American Journal of Diseases of Children

VOLUME 46 SEPTEMBER, 1933 NUMBER 3

PHYSIOLOGY OF CEREBRAL ACTIVITY IN CHILDREN AS A NEW SUBJECT OF PEDIATRIC INVESTIGATION

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The present epoch of pediatrics is characterized by ever-growing interest in the psychic life of the normal and the pathologic child. The pediatrician of today is not only the healer and the preventer of disease, but also a good advisor in the complex problems of the behavior, mental hygiene and education of the child. It is well known how often psychic disorders evoke bodily diseases and, on the other hand, how often somatic causes produce disturbances of the psychic life, especially in the growing organism. Furthermore, some psychopathies manifest themselves at a tender age, and their initial symptoms, early diagnosis and prophylaxis represent a most important problem for pediatric investigation. Pediatricians, therefore, have a vital interest in the psychology and psychopathology of childhood. They have contributed much to the scientific progress of these domains of science and participated in the creation of the contemporary scientific teaching of education.

During the last thirty years, however, a new branch of the natural sciences has arisen, namely, the physiology of the highest nervous activity in man and in animals. This has opened unlimited horizons for pediatric and psychiatric investigation.

The idea that the brain is an organ of reflex activity was first suggested by Dr. I. M. Setchenov in 1863, and then in 1901 was brilliantly developed by Prof. I. P. Pavlov in experiments on conditioned reflexes on animals.

Twenty-five years ago, I made the first attempt to investigate the highest nervous activity of a child by a strictly physiologic method. At that time there was little or no knowledge of the physiology of the child's brain, and that of the psychic processes consisted exclusively of psychologic observations and experiments. The absence of a general outline of the physiologic activity of the brain and the ignorance of the fundamental rules which govern this activity were great obstacles to the correct understanding and biologic interpretation of the various manifestations of psychic life in children.

Read at the Annual Meeting of the American Pediatric Society, Rochester, Minn., May 28, 1932.

The first experiments on children showed that the law of formation of the conditioned reflex connections remains true for human beings. Very different external agencies could be conditioned, and acquired the capacity of eliciting any reflex activity (motor, secretory, emotional, etc.) if they were made to coincide a certain number of times with this activity.

The cortical reflexes in children are temporary, individual, acquired reactions which can be established and can function only under definite conditions; they are conditioned reflexes. The conditioned, cortical reflexes are based on the infracortical, native reactions characteristic of the species and elicited under any conditions; these extracortical reactions are called unconditional reflexes. To the unconditioned reflexes belong such complex system reflexes as instincts, "affects" and emotions.

The mechanism of the conditioned reflex is the instrument of the highest adaptation of the child to his surroundings. By means of incessant conditioning to external situations, the child establishes the most precise and expedient adjustment to the ever-changing conditions of the outer world.

Soon in the course of investigation cortical reflexes from all the receptive organs of the child were established. The most varied optical, acoustic, olfactory, thermal and mechanical skin stimulations were easily conditioned, and began to evoke definite reflex activity (motor, secretory, emotional, etc.) if they were made to coincide several times with this activity.

Conditioned reflexes to the internal stimulations which arise in the organism itself were also established. For instance, it was possible to form conditioned reflexes to the interoceptive impulses issuing from the motor organs. Every posture or movement soon began to elicit the conditioned salivary response, if these stimuli had been reenforced several times by feeding.

Thus not only the agencies from the outer world, but also the innumerable impulses originating in the organism itself, become easily conditioned and acquire the ability to elicit just those activities with which they have several times coincided. These internal conditioned reflexes are incessantly differentiated and integrated by the cerebral cortex into coordinated conditioned reflex systems, and make possible the subjective analysis of reactions arising in the organism itself. Undoubtedly they enter, as an important integral part, into the physiologic mechanism of those complex subjective processes which are called emotions. In fact, a conditioned and unconditioned reflex act is in no instance an isolated reaction but evokes changes in the various organs and tissues of the organism. These changes are the source of manifold interoceptive excitations, which run back to the subcortical centers and

cerebral cortex and there are analyzed, integrated and connected with the initial reflex arc into a coordinated conditioned reflex system. Afterward the conditioned stimulus itself becomes able to elicit the whole integrative reflex effect of this interoceptive conditioning. Thus, the emotion is an integrated subcortical reflex effect which develops as a result of synthesis of the internal impulses arising in the organism itself under the influence of the unconditioned or conditioned reflex act. Therefore there are conditioned and unconditioned emotions, depending on whether they are evoked by conditioned or unconditioned stimulation.

In the cerebral hemispheres enormous inhibitory activity develops. The cortical inhibitions either are strictly localized reactions or manifest themselves as generalized phenomena. In the first case they have all the characteristic features of the conditioned reflexes; they may be elicited by the varied external and internal stimuli; they are individual, acquired reactions, which are established and function only under definite conditions. In the second case cortical inhibition is exhibited in a general decrease of excitability of the cerebral cortex and in the development of the inhibitory phasic states, as for instance narcotic, paradoxical, ultraparadoxical and hypnotic phases.

FORMS OF INTRACORTICAL INHIBITION

The following forms of intracortical inhibition are distinguished:

External inhibition, produced by the sudden action of some new strong external agent.

Interoceptive inhibition, inhibition of the cortical reflexes by stimulations originating in the organism itself, e. g., by overfilling of the bladder or rectum.

Conditioned inhibition, the form in which an indifferent agent becomes negatively conditioned and acquires the capacity of inhibiting the conditioned positive reflex, if the combined action of this agent with the positive stimulus is left several times without reenforcement. The mechanism of conditioned inhibition is a powerful regulator of the highest nervous activity in children. By means of this mechanism every conditioned activity can be stopped at once. From the earliest age the mother, nurse and other persons following the rules and the traditions of religion, family and society establish endless conditioned inhibitions which regulate the behavior of the child. Later school and civilized society perfect the inhibitory systems and create a personality which is capable of developing the most expedient adjustment to the various and difficult conditions of life. The man possessing strong conditioned inhibitions is the master of his instincts and emotions.

Recently some new facts have been learned concerning another important form of intracortical inhibition, i. e., so-called conditioned trace reflexes. As is well known, human behavior is continuously

adapted to future situations, and this anticipatory type of adjustment assumes an enormous importance in human life. If a simple conditioned reflex enables the child to respond in a preparatory way to approaching situations, the anticipatory adaptation attains the highest degree in the mechanism of the conditioned trace reflex. Here the external or internal stimulations become signals of a sometimes very distant future action. The cortical trace reflexes are established under such circumstances that the reenforcement (feeding) takes place a long time after the conditioned signal stimulation has already ceased to act. The trace responses in children as compared with animals are extreme subtle and specific reactions. Their trace periods, i. e., the intervals of time between the end of the conditioned stimulation and the moment of the reenforcement, may be made very long—minutes or even hours —without any observed disturbances in the adjustment to the time conditions. The study of trace reactions is of special interest, as it is in reality the investigation of the cortical functions during the state of prolonged "expectation." As is well known, Prof. I. P. Pavlov proved long ago that the establishment of trace reactions is based on the development of central inhibition. Further investigation of trace reflexes in children completely verified the inhibitory origin of these reactions in human beings; the conditioned reflex arc is entirely inhibited during the trace period of the reflex (Dr. V. A. Leonov). Recently, however, new facts have been learned which increase the knowledge of the dynamic conditions in the cerebral hemispheres during the development of the trace reaction. In a series of experiments Dr. A. J. Machtinger and Dr. S. L. Levin have shown that the inhibition which develops in the conditioned reflex arc during the trace period induces strong excitement in the other parts of the cerebral hemispheres. These authors introduced neutral agencies into the trace period of a well stabilized reflex, and found that under these conditions the agents acquired irritative functions; at the same time the inhibitory stimuli (e. g., the inhibitory differentiations), on their introduction into a trace period, no longer inhibited. The excitement is usually greater when the trace periods are longer. It is especially strong in those children who show, in general, weak inhibitions. These experiments show how unfavorably the general activity of the brain is affected by the state of prolonged "expectation." The latter produces a general excitement of the cerebral hemispheres and leads to a decrease in the differentiating and regulating functions of the cerebral cortex. Thus the exactness of everyday life represents, from the physiologic point of view, a favorable hygienic factor in the function of the whole central nervous system.

The other forms of intracortical inhibition are the extinction, differentiation and delaying of conditioned reflexes, the inhibition produced by exhaustion and toxic causes, the inhibition evoked by intense infracortical excitations and the inhibition in hypnosis and sleep. All these seemingly different forms of inhibition are accepted as one and the same nervous activity, which is due to a decrease of excitability of the cortical cells.

The problem of inhibition has remained unsolved. However, I think that all the facts known concerning the cortical reflexes can be more satisfactorily understood if one assumes that there exists only one indisputable attribute of the cortical cell, namely, its excitability. While the optimal excitability is an ideal condition for cortical reactions, hyperexcitability causes the cortical cells to respond to the stimulations with abnormally increased reflex effects; this leads inevitably, on its own account, to the violation of laws of expediency and economy. However, when either local or general excitability of the cerebral hemispheres drops below the optimal level, there develop various local or general inhibitory phenomena. At present many intermediate states of decreased excitability are known, in which the cortical cells maintain the capacity to respond to stimulations, but these reactions show definite quantitative and qualitative changes. As soon as the decrease of excitability attains a certain degree the cortical cells cease to conduct impulses and to respond to stimuli. In children the state of the decreased excitability may last for minutes, hours and even days.

In some cases, however, inhibitory phenomena can be evoked by positive stimulation of the antagonistic innervations. In fact, every motor flexion reaction may be stopped by the conditioned stimulation which elicits the activity of the antagonistic extensor muscles. Here the primary process is the positive antagonistic reflex and only secondarily a decrease of excitability of the previously acting centers develops (inhibition by induction).

The study of conditioned reflexes shows that any degree of excitability of the cortical cells can be evoked by means of conditioning. The conditioned stimulus elicits, as a rule, just that state of excitability which existed in the cortical cell during its action. Therefore every neutral agent can be transformed into a stimulus, which evokes in a reflex fashion a definite degree of increased or decreased excitability in the cortical cells. This enables one to understand not only inhibitory phenomena, but also other important facts, which I shall now consider.

The cerebral hemispheres, which are the organs of highest adaptation, produce not only inhibitive but also on a wide scale accelerative activity. Recently an experiment was conducted by Dr. A. J. Fedorov which made possible the investigation of the cortical mechanism of

acceleration. This experiment has shown that cortical acceleration is strictly conditioned. Every neutral agent may be transformed into a conditioned accelerator, provided it has repeatedly been made a signal of the immediate release and instant reenforcement of the subsequent conditioned reflex.

The following example shows the establishment of conditioned acceleration in a normal child:

CASE 1.—A girl, aged 8 years, had a conditioned optical reflex to a red light, which was usually reenforced at the thirty-first second of stimulation. The conditioned secretory response developed, as a rule, from six to seven seconds after the commencement of the stimulation. When the optical reflex had been well stabilized, another stimulus was introduced into the experiment: the sound of a buzzer, which I desired to transform into a conditioned accelerator. The sound

The Mechanism of Acceleration

Date	Time, Min.	Stimulation	Latency of Salivary Reflex, Sec.
Before Training (the sound of the buzzer produces indifferent response)			
6/ 6/31	..	Sound of buzzer; 5 seconds later, red light.....	8.3
	3	Sound of buzzer; 5 seconds later, red light.....	7.4
	3	Red light	7.0
After Training (sound of buzzer is a conditioned accelerator)			
6/13/31	..	Red light	9.5
	3	Sound of buzzer; 5 seconds later, red light.....	1.0
	4	Sound of buzzer; 5 seconds later, red light.....	1.2
	7	Red light	4.0
6/ 9/31	..	Red light	6.2
	3	Sound of buzzer; 5 seconds later, red light.....	0.5
	3	Red light	11.4

of the buzzer was used in the following combination with the optical stimulus: the sound of the buzzer (during five seconds), a pause (five seconds) and then the red light, which was immediately (in from three to five seconds) reenforced by giving the child sugared cranberries. This combined stimulation was alternately applied with stimulation by the red light alone, but in this case the child received food, as before the introduction of the sound of the buzzer, i. e., thirty seconds after the commencement of the red light. After several such trials the sound of the buzzer, to which the child had previously been quite indifferent (see table), now began to evoke a short motor response and some drops of saliva. However, it soon ceased to produce these reactions, but acquired the new property of accelerating the reflex to the second stimulus. Now the red light, when it was preceded by the sound of a buzzer, evoked the salivary reflex in from five-tenths to one and two-tenths seconds after the commencement of the stimulation, whereas, when applied alone, it elicited the conditioned secretion no sooner than in from four to eleven and four-tenths seconds.

Thus, the sound of the buzzer, to which the child had previously been quite indifferent, now became a stimulus of acceleration. The speed of development of the secretory reflex to the red light, used in

successive combination with the sound of the buzzer, attained a degree that was never observed under other conditions.

Cortical acceleration is based, seemingly, on the anticipatory increase of excitability of the conditioned reflex arc, produced by a conditioned accelerator. As is known, the maximal excitation of the cortical cell is observed just at the moment of application of the conditioned stimulus. Then, with every second this excitation gradually decreases, owing to the development of inhibition as a defensive process, protecting the extremely reactive cortical cells from fatigue. In the experiment the accelerating stimulus coincided consistently with maximal excitation of the conditioned reflex arc, for this reflex in combination with the accelerator was always immediately reenforced by the unconditioned activity. After a number of such coincidences the first stimulus becomes able itself to evoke the state of maximal excitability in the cortical cell of the second reflex. Thus, in the mechanism of conditioned acceleration there is a coordinated system of two successive stimuli, one after another, the first of which acquires, by means of conditioning, the ability to increase excitability and facilitate conduction in the conditioned reflex arc of the second reflex.

The function of the mechanism of conditioned acceleration varies in different children. In some pathologic cases, e. g., in children with a hypo-excitable nervous system, especially in myxedema, it is so weakened that the accelerating effect cannot be achieved.

LAWS OF CONDITIONED REFLEX ACTIVITY

At the present time a number of rules regulating conditioned reflex activity in children are known; one of these is the law of intensity.

The magnitude of cortical reflexes depends on the intensity of conditioned stimuli. Under the condition of an optimal cortical and infracortical excitability, stronger conditioned stimuli elicit in a normal child more intense reflex effects than weaker stimuli. The greater the energy entering the hemispheres the more intense is the conditioned reflex response.

There exists a definite optimal intensity for conditioned stimuli when they evoke the more intense reflex effects. The limits of this optimum vary in different children; as soon as these limits are overstepped, the further decrease or increase of intensity leads only to a diminution of the magnitude of the cortical responses.

Thus the normal adaptive work of the cerebral cortex is characterized by extreme economy in the expenditure of nervous energy. Under conditions of optimal reactivity the nerve cells spend just so much energy as corresponds to this intensity of the stimulus.

Another important rule is the law of order. The experiments of Dr. N. N. Derevtshikova with children have shown that the order of sequence of the stimuli greatly influences the conditioned reflex effects. During the work with cortical reflexes, constant results may be obtained only on the condition that the stimulations follow one another in a strictly definite order. As soon as this order is disturbed, the magnitude of the reflexes immediately decreases and the reflex effects become irregular.

The positive stimuli, applied in a changed order of sequence during the periods when the inhibitory stimuli were previously tested, are inhibited; on the other hand, the inhibitory stimuli, which are tried at the periods when the positive stimulations usually took place, elicit positive reflex effects, i. e., do not inhibit.

Thus, any change of the once established order in sequence of the stimuli produces a functional disturbance. In normal children, however, if the new conditions become more or less constant, the stabilization of new modifications and the reestablishment of a new dynamic equilibrium proceed very quickly.

Thus, regularity and strict order in the sequence of stimuli are the fundamental conditions facilitating and improving the work of the brain.

The next general rule is the law of "proximity." If several conditioned stimuli, signalizing one and the same unconditioned activity, either systematically follow one another or are successively joined to each other, the conditioned response is elicited only by the stimulus proximate to the reenforcement, while all the other stimuli gradually lose their stimulating action.

Children transmit the conditioned response to the proximate stimulus with varying speed. Whereas in normal children the adjustment to the proximate stimulus is definite, in neuropathic, especially in hyperexcitable, patients it is unstable, being often disturbed by various, sometimes insignificant external or internal causes. Children with lowered cortical function show a marked retardation in the development of this adaptive process.

Adjustment to the proximate stimulus has often proved to be disturbed by fatigue. Many times delay in this adjustment occurs toward the end of the experiment, when children complain of being tired.

One of the fundamental laws is the law of time. As early as 1912 it was proved by Dr. J. P. Feokritova, in Professor Pavlov's laboratory, that "time," as such, may be conditioned in dogs. The factor of time greatly influences the cortical reflexes in children. Without paying attention to this factor it is impossible to obtain uniform results. The experiments of Dr. N. N. Derevtshikova and Dr. A. J. Fedorov

on children have shown that if the conditioned food reflexes are tested at regular intervals, the conditioned secretion appears exactly at the moment of the test, even if stimulation is lacking.

Recently Dr. A. J. Machtinger has proved in children that the law of time remains true also with regard to the inhibitory stimuli. Every interval of time could be negatively conditioned and inhibit the positive reflex if this reflex, which had been tested at this interval, was systematically left without reenforcement.

The law of time is so universal that it even keeps its power in some cases of idiocy.

The study of cortical reflexes revealed a fact which is very important from the practical point of view: that the reactivity of the cerebral hemispheres does not remain constant even in healthy children, but fluctuates under the influence of manifold external and internal conditions. Often the changes in the behavior of a child noticed by his family and at school and elsewhere are evoked by these fluctuations of cortical reactivity. At the present time many characteristic phasic states are known which influence the general behavior of the child. When the cortical cells and corresponding infracortical centers show an optimal excitability, the cortical reactions are intense and quick, and follow the laws of intensity, order, proximity and time.

However, if the optimal excitability is changed, children begin to react otherwise. The increase of excitability leads to the development of two characteristic phasic states. In the first or simple excitatory phase, the positive conditioned reflex effects are markedly increased, but all the fundamental laws retain their significance. The inhibitory cortical regulation is normal. Thus, the adaptive work of the cerebral hemisphere is subtle and precise, but all the nervous reactions have a higher level than in the optimal state.

The second or leveling excitatory phase comprises the cases in which the reactions are hyperintense and do not follow the law of force; here the weak and strong stimuli produce equally intense conditioned reflex effects. During this phase the inhibitory functions of the cerebral hemispheres are decreased and the inhibitory reflexes often prove to be disinhibited. This state undoubtedly represents a pathologic condition, forming a physiologic basis for some cortical neuroses, e. g., neurasthenia.

In another direction from the optimal state a series of inhibitory phases exists, which presents gradual transitions from the optimal reactivity to complete general inhibition, i. e., sleep. Here one distinguishes the narcotic phase, in which the magnitude of the conditioned reflexes is diminished but the law of intensity is retained.

A further decrease of excitability leads to the development of the leveling inhibitory phase, in which strong and weak stimuli evoke feeble responses of the same magnitude.

The next paradoxical phase shows profound qualitative changes in cortical reactivity. During this state weak stimuli elicit more intense reflex effects than stronger ones. The strong stimuli are here overmaximal for the cortical cells, and either evoke decreased responses or remain without any reflex effect. The paradoxical form of reaction is an indication of weakness of the cerebral cells and is often observed in infants and in hysterical patients.

In pathologic cases there develops another ultraparadoxical phase, in which positive conditioned stimuli produce the inhibitory effects, whereas the inhibitory stimuli elicit the positive conditioned responses (negativism).

Of great practical importance is the hypnotic phase, in which the cerebral hemispheres are in a state of general inhibition with the exception of some definite waking points. The study of conditioned reflexes in children during a hypnotic trance contributed greatly to better knowledge of the function and dynamics of this state. The experiments of Dr. S. L. Levin have shown that some conditioned reflexes, e. g., acoustic ones, which have been established can be easily evoked also in hypnosis, whereas others, e. g., cutaneous reflexes and especially the conditioned flexion reflexes, are either greatly decreased in a hypnotic trance or cannot be elicited at all. Obviously, during a hypnotic trance the acoustic analyzer is comparatively free from inhibition and open to stimulation, whereas other analyzers are deeply inhibited. The cerebral cortex is in a state of segregation.

Then the question arose: Is the establishment of the new conditioned reflexes possible during a hypnotic trance? The experiments gave a positive answer. New conditioned connections could be established even in a deep hypnosis, but there was also a great difference among different analyzers; while the acoustic reflexes could be established relatively quickly, the formation of the conditioned skin responses and the flexion reflexes required a great number of reenforcements.

It is an important fact that the conditioned reflexes could be established in a hypnotic trance even under the conditions of a complete amnesia. In this case, however, the conditioned reactions did not enter into the general synthetic work of the cortex, but remained co-conscious. The children elicited the conditioned responses, being completely unaware why they did so; at the same time they motivated very well their actions with regard to the reflexes which had been established during a waking state.

During a hypnotic trance it was possible to establish not only new conditioned positive reflexes, but also new inhibitory reactions. However, the cortical negative reflexes were formed much more slowly in hypnosis than in a waking state. For instance, if the conditioned inhibition was established in the children in a waking state after no more than from two to four nonreenforced trials, during a hypnotic trance it was necessary to perform fifty or more nonreenforced stimulations in order to obtain some inhibitory effect. The conditioned inhibition established in hypnosis is very unstable and its inhibitory effect untrue. Often the negative stimulus does not inhibit the positive reflex but, with an increase in the depth of hypnosis, even evokes the positive reflex effect. The inhibitory process is more inert here than in a waking state; this is proved by the fact that the inhibitory stimulations leave lasting after-effects in hypnosis. All these facts show

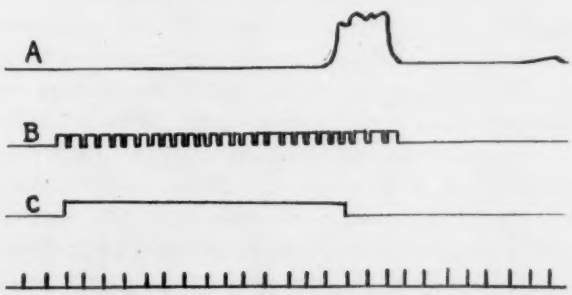

Chart 1.—*A*, motor reflex on opening the mouth. *B*, response to stimulation of the skin. *C*, response to a metronome.

that in hypnosis the work of the waking, functioning fields of the cerebral cortex is deeply and qualitatively changed.

In a hypnotic trance the excitability of the acting cortical fields shows great fluctuations, depending on the depth of hypnosis. Here all the variations of phasic reactivity may be observed from the intense excitatory states, in which very stable conditioned connections are sometimes formed, to the profound inhibitory phases, immediately passing over into sleep. One or another inhibitory phase could be produced by making the hypnotic state deeper or weaker. This is illustrated by the following case.

Case 2.—In a normal boy, aged 11 years, the conditioned positive reflex to the metronome and the conditioned inhibition to this reflex from the mechanical stimulation of the skin were established during a hypnotic trance. The metronome elicited the conditioned motor and salivary reactions and the stimulation of the skin inhibited both of these reactions completely. However, as soon as the hypnotic state attained a definite depth, there appeared regularly an ultraparadoxical reactivity: The inhibitory agent, the cutaneous stimulation, began to evoke a

positive motor response, whereas the positive agent, the metronome, did not produce any conditioned reflex effect (chart 1). If the hypnosis was still deeper the child fell asleep and all conditioned reflexes disappeared. On the other hand, if the hypnotic state was weakened, the metronome again acquired a positive action and stimulation of the skin began to inhibit the reflex. The child showed post-hypnotic amnesia and was absolutely unaware of the existence of these reactions and manipulations. Thus, by increasing or decreasing the depth of hypnosis, different phasic states of cortical reactivity could be evoked, and it was possible to observe the gradual transition from one phase to another.

The dynamics of the waking cortical fields in hypnosis are characterized by wide irradiations of excitation and inhibition, by the decrease of concentration and reciprocal induction. As a result of these dynamic changes the specificity of cortical reflexes decreases, and those external stimuli which did not evoke reflexes in a waking state elicit positive responses in a hypnotic trance. The decrease in the process of concentration leads to the lowering of the differentiating functions of the active fields of the cerebral cortex. With an increase of the depth of hypnosis these changes become more definite.

Thus, all these experiments have yielded the absolute evidence that during a hypnotic trance the cerebral cortex is in a segregated state; some fields are in a waking condition and are open to stimulation, whereas others show a very low excitability and do not respond to stimulation. On the other hand, the facts have been determined which characterize the function of these isolated fields when they work without the influence and control of the cerebral cortex as a whole. During hypnosis the new conditioned positive and inhibitory reflexes can be established even under the conditions of a complete amnesia, but the formation of the conditioned connections proceeds here much more slowly than in a waking state. The conditioned reflex effects are unstable and untrue. Wide irradiations of excitatory and inhibitory processes, decreased concentration and induction and lasting inhibitory after-effects characterize the dynamics of the segregated cortex. However, if the depth of hypnosis attains a definite degree of intensity, the inhibition develops also in the waking fields of the cortex; then the conditioned responses show an inhibitory phasic reactivity, or sometimes the reflexes of the second order appear. As is known, the latter symptom is a typical condition in severe idiocy. Thus, the work of the waking fields, isolated from the influence and control of the cerebral cortex as a whole, shows all the features of insufficiency that are observed in severe pathologic cases.

The conditioned reflexes, having been established in the completely segregated cortex, do not enter into the general integrative work of the cerebral hemispheres and remain co-conscious. The children perform the conditioned reflex acts, unaware why they do so. Thus the

problem of "subconscious intelligent adaptation" and "unconscious" action becomes the subject of strict physiologic investigation, which gradually discloses the biologic nature of these phenomena.

I made an attempt to apply the conditioned reflex technic to the physiologic study of speech. Dr. N. R. Shastin has proved that every verbal stimulus may be made conditioned and can elicit any positive or inhibitory activity if it has coincided several times with this activity. From the physiologic point of view, every simple sound in any language is a simple acoustic conditioned stimulus, every word is a conditioned reflex complex and every sentence is a conditioned system of complexes. Innumerable idioms used in speech may serve as a typical example of well stabilized conditioned reflex systems. Usually ideas are expressed by means of more or less stabilized conditioned verbal systems, which really form the framework of the language. In writing and reading, a letter represents, correspondingly, an optical conditioned stimulus, a written word, a conditioned reflex complex, and a sentence a conditioned reflex system. Undoubtedly in quick reading and writing, one works with conditioned reflex complexes and systems. Thus the whole process of learning to speak, read and write is physiologically the process of a complex conditioning.

The experiments of Dr. N. R. Shastin, A. B. Volovic and N. N. Derevtshikova have proved that the fundamental laws of the simple conditioned reflex activity remain true also for the complex stimuli and their systems. The conditioned verbal reflexes can be accelerated, differentiated, delayed and inhibited as simple conditioned responses.

The verbal systems, like all other conditioned reflex systems, are in a mobile dynamic equilibrium, which exists as long as the construction of the system remains constant. But as soon as the conditions are changed, e. g., when the order of sequence of the words is altered, the function of the verbal system becomes deranged and the conditioned reflex effects are inhibited. However, in normal children such inhibitions are of a very short duration and the new equilibrium establishes itself quickly.

The study of the relative physiologic significance of separate words composing the verbal reflex system (the sentence) has shown that the subject elicits, as a rule, a more intense conditioned response than the predicate or object. Thus, physiologically, the subject is the dominant ingredient in the conditioned verbal system.

In a series of experiments the conditioned reflex connections in verbal associations have been studied. These experiments have proved (Dr. A. J. Fedorov) that if one word of an association is conditioned, all other words belonging to this association also become conditioned and evoke the same conditioned response. For instance, an association

of six words, pigeon-turkey-hawk-owl-hen-swallow, was established by systematic repetition of these words; and one of them (pigeon) was made to coincide with feeding; all the words of this association were thus conditioned. Each of them elicited the intense motor and salivary conditioned response, while all words meaning other animals or objects, trees, fruits, etc., were absolutely inactive. Then the names of the other birds were used, but did not evoke any conditioned responses. Obviously, there were no reflex connections among stimuli belonging to the same group unless these connections were especially established by means of conditioning. On the contrary, rather intense conditioned secretion was elicited by stimulation with the word "a bird," i. e., by the word signifying the general concept in this case. The fact that this word at once evoked the positive conditioned response without previous reenforcement with feeding proves that a direct conditioned reflex connection exists between the group word and the ingredients belonging to this group.

The positive or inhibitory reflex effects of the verbal stimuli are absolutely conditioned. Every word or sentence which elicits a positive conditioned response can be transformed into a negative, inhibitory stimulus if it has been left a certain number of times without reenforcement. This can be illustrated by the following experiment: As is known, the phrase "You may" serves in life as a positive stimulus and results in some action. On the contrary, the phrase "Do not" has an inhibitory meaning and stops the conditioned reactions. This fact was observed well in experiments with salivary secretion. Dr. N. R. Shastin, having joined the words "You may" to another positively acting stimulus, received in all cases the positive conditioned response; however, as soon as he had joined to the positive stimulation the phrase "Do not," the conditioned reflex was at once inhibited. Then an attempt was made to transform the words "You may" into an inhibitive stimulus and the phrase "Do not" into a positive one. For this purpose the child was given food when he was being stimulated by the phrase "Do not," and the reflex was not reenforced when the words "You may" were joined to the conditioned stimulation. Under these conditions the phrase "Do not" lost its inhibitory power very quickly, i. e., after three reenforced trials, and then began to elicit the conditioned motor and secretory response (chart 2). On the other hand, it was much more difficult to make the positive words "You may" inhibitory conditioned. This phrase had to be left fourteen times without reenforcement until it began gradually to have a definite inhibitory effect (chart 3). It is thus seen how easy it is to spoil even stabilized inhibitory stimulation, and how much more difficult it is to transform an inhibitive agent into a positively acting stimulus.

Of special interest are the experiments in which the verbal stimuli introduced conflict with the facts which they signified. For instance, if a child is stimulated simultaneously by the red light, which has been previously made conditioned, and by a contradictory phrase, "There is no red light," he responds to this combined stimulation with the positive conditioned motor and secretory reaction. Thus the competition between the actual and the contradictory verbal stimuli results in the victory of the acting agent; the actual stimulation overcomes the verbal one, which contradicts it. Therefore in normal children real surroundings cannot be distorted by verbal stimulations, as, however, often occurs in pathologic cases, e. g., in hysteria.

Chart 2.—Curve showing transformation of "Do not" into a positive stimulus.

On the basis of the knowledge of the cerebral functions a general outline of the physiologic activity of the brain can be given.

All the results obtained in the study of the conditioned reflexes prove that the work of the cerebral hemispheres is a highly coordinated "system" activity.

Having worked in Prof. I. P. Pavlov's laboratory on the problem of localization, I was led, in 1911, to the concept of the unity of the constructive plan of the cerebral cortex. Experiments with extirpation of different parts of the cerebral hemispheres showed that the cerebral cortex, including the motor zone, is an immense receptive surface, the analyzers being an accumulation of specific elements concentrated in definite fields of the cortex.

Thus, if the study of the conditioned reflexes confirmed in general the old teaching of localization, it established another fundamental concept, that of the temporary conditioned character of the cortical localization within the analyzers.

CORTICAL REFLEX SYSTEMS

The cerebral hemispheres have a great mass of reserve combining cells, which are real connectors for the establishment of ever new conditioned reflex connections, conditioned reflex complexes and systems of complexes. The cortical systems are initiated in the receptive cells of analyzers, immediately connected with peripheral receptive organs, but the whole mass of the connecting and combining cells of the cerebral hemispheres takes part in their formation. By the intermediate work of these cells the most intricate connections and combinations of the cortical elements, belonging to one or several analyzers, may be obtained. The extreme development of this combining tissue in the brain of the human being makes possible the formation of the most extended and

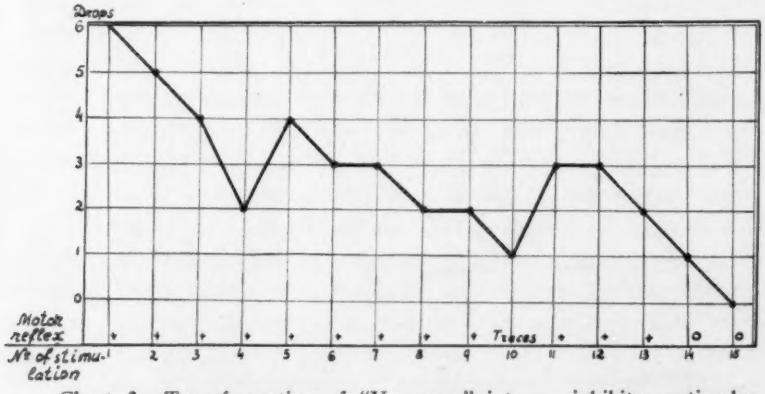

Chart 3.—Transformation of "You may" into an inhibitory stimulus.

intricate conditioned reflex systems, serving in the highest analytic and integrative work of the brain.

The cortical systems are acquired, individual localizations, constantly changing their structure under the influence of environmental conditions.

Some of the cortical reflex systems function as allied, agonistic innervations, and are capable of simultaneous combined action. Other systems are antagonistic to them, and can function only in successive combinations with the reflex systems of the first group. Some of them develop positive, others inhibitory, reflex effects.

The allied systems are dynamically in irradiative interrelation; an excitation or an inhibition originating in one of them spreads over the others, involving them in the same process. The allied systems are in inductive interrelation with the antagonistic systems; every excitation arising in the allied systems induces inhibition in the antagonistic systems and vice versa. In the normal brain the allied and

antagonistic systems are perfectly coordinated, and their dynamic interaction is well balanced.

The cortical cells have the fundamental capability of fixing and retaining the established system connections for a certain period of time, and this capability is one of the most important factors determining the quality of the cortical work. The resistance of the cortical reflex systems to the time as well as to the other external and internal influences depends on the degree of stabilization of the systems and the individual quality of the cortical cells.

The excitations arising in the cortical reflex systems, which have one and the same effector cell, compete with one another for the possession of the pathways to the effector element. In this struggle the degree of stabilization of the conditioned reflex systems plays a great rôle. Under the same conditions the excitations of the old, well stabilized systems conquer the excitations arising in the newly established systems.

The cortical systems do not remain constant in their structure, but either enrich themselves continuously with new ingredients or lose them, owing to changes in the environmental conditions. Into the structure of the cortical reflex systems not only the positively but also the negatively acting elements may enter, the stimulation of which decreases the excitability of the whole system and makes it inactive. A typical example is the so-called conditioned inhibition, in which the stimulation of one inhibitive element interrupts the conduction in the whole system.

The cortical reflex systems have fluctuating thresholds of excitation, an "excitation-*Bereitschaft*," which depends on the frequency and the time of stimulation, the distribution of excitations in the remaining cortex and the excitability of the corresponding infracortical centers with which they are connected.

In a waking state the cerebral cortex functions as a whole; it performs an analysis and synthesis of impulses arising from three chief sources: the exteroceptive impulses from the outer world, the interoceptive impulses from the organism itself and the impulses arising in the associative activity of the preformed conditioned reflex systems. In reality, every conditioned stimulation eliciting a definite reflex act is synthesized with all the interoceptive stimulations which originate in the whole organism as a result of this act. These internal impulses run back to the cerebral cortex, and are analyzed and integrated there into the conditioned reflex systems. This process of internal conditioning represents the physiologic counterpart of those subjective states which accompany every conditioned response. On the other hand, every new conditioned reflex arc becomes a new ingredient in the framework of the previously established conditioned reflex systems, and therefore its excitation involves all the preformed systems in a mutual integrative activity.

In early childhood, when the conditioned reflex systems are poor in number and more simple in structure, cortical analysis and synthesis are rather limited. However, every year with the incessant formation of new and more intricate cortical systems the analytic and integrative activity of the cerebral hemispheres becomes progressively more subtle and complex, and attains its highest level during the period of education.

Dynamically, the function of the cerebral cortex is strictly coordinated with the activity of the infracortical nervous system. Even the most insignificant change of excitability in the subcortical centers immediately evokes corresponding changes of excitability in the cortical systems, which are connected with these centers.

The most regular and precise cortical reflex effects are obtained when the subcortical excitability is optimal. With regard to the conditioned food reflexes this is the case when children have a healthy appetite at the right hour before the meal. However, as soon as the subcortical centers become either hypo-excitable or hyperexcitable, the excitability of the corresponding cortical fields decreases in both cases, whereas the conditioned reflexes diminish in magnitude or disappear entirely. For instance, after satiation, when the excitability of the subcortical food center is low, the magnitude of the conditioned salivary reflexes is markedly diminished. On the other hand, infracortical overexcitations have the same deleterious effect on the cortical reflexes. When the interval of time between meals is lengthened by many hours, as soon as the overexcitation of the food center attains a definite degree of intensity the magnitude of the conditioned food reflexes diminishes and the reflexes become more generalized and then disappear entirely. Everyday experience shows that the intense effects, being strong infracortical reactions, stop the whole analytic and synthetic work of the cortex at once, markedly decreasing the regulating function of the cerebral hemispheres.

The definite distribution of excitations in the infracortical parts leads indispensably to the adequate distribution of the excitability in the cerebral cortex. All the processes of irradiation and reciprocal induction arising in the infracortical regions are immediately projected in the cerebral hemispheres and evoke the corresponding dynamic changes in them.

Thus the dynamics of the cerebral cortex is strictly coordinated with the dynamic processes of the infracortical regions, and the precise and flexible balance between them is the fundamental condition for the normal work of the brain.

Physiologic study of cerebral activity furnishes vast material on the characteristics of the various types of children. For the differentiation of types the dynamic principle already mentioned is accepted, i. e.,

the dynamic interaction between the cerebral hemispheres and the extracortical nervous system. The following four fundamental types of children can be distinguished on the basis of this principle.

TYPES OF CHILDREN

The first is the central well balanced type, in whom the normal infracortical processes are perfectly regulated and balanced by the strong cortical activity. The children of this type show an ideal dynamic coordination of cortical functions with subcortical activities. They show an excellent adaptation of their instincts and unconditioned emotions to the ever-changing requirements of the surroundings. In these children the cortical positive as well as inhibitory reflex effects are intense, and the conditioned reflex connections are stable and quickly established. If the phasic reactivity develops, the extreme phases are of short duration and the optimal excitability is quickly reestablished. The unconditioned reflexes are also of a normal magnitude, and are perfectly regulated by cortical influences. The powerful cerebral cortex and normally excitable infracortical regions create the most favorable conditions for the cortical productivity. Normal infracortical excitations charging the corresponding cortical cells with energy greatly contribute to the optimal function of the cerebral hemispheres.

To the second subcortical type belong children in whom the infracortical processes have the upper hand over the cortical influences. In these cases the hyperexcitable extracortical nervous system is not sufficiently regulated by the cerebral cortex. The inert, powerful infracortical activities, e. g., the instincts or unconditioned emotions, cannot be adapted to the surroundings satisfactorily by a conditioning process, but, being insufficiently suppressed by the cerebral cortex, they often dominate and determine behavior. Under experimental conditions these children often show incessant, irregular movements and intense intermediate salivary secretion. At the same time the conditioned positive reflex effects are usually relatively weak. The inhibitory functions of the cerebral hemispheres are lowered. The extinction of reflexes is slow, the conditioned inhibitions and delayed and trace reactions are unstable and their reflex effects untrue. Fluctuations in cortical reactivity are characteristic. As soon as some difficult task arises before the child, extreme excitatory or inhibitory phases develop, which sometimes persist for days and even weeks. As the periods of excitatory and inhibitory reactivity are of long duration and alternate with one another, the cerebral work exhibits a definite cyclic periodicity. The children of the subcortical type show an inconstant character and are unable to be master of their instincts, affective states and emotions. In experiments with stimulation by the external agencies, evoking defense

reactions, e. g., by slight electric current or by pressure on the eyeball, such children have shown a very low threshold, an intense, widely generalized defense reaction and a lasting excitatory after-effect; under the same conditions the children of the central type show a high threshold, limited motor response and short after-effect. Although the predominance of the subcortical processes handicaps the work of the cerebral hemispheres, the children are usually able to learn satisfactorily in school, having difficulty only in their instinctive and emotional adjustment. The discord of the dynamic coordination between the cerebral cortex and the extracortical nervous system is the greater the more hyperexcitable are the infracortical centers or the weaker are the influences from the cerebral hemispheres. Depending on these factors, there are all the variations from hot-tempered but capable and sometimes even creative persons to those who are mentally nonproductive and entirely in the power of their passions and instincts. Neurasthenia and psychasthenia are neuroses which frequently occur in these cases. It is an important problem whether manic-depressive psychosis is not the further, progressive development of the fundamental characteristics of this type.

The third is the cortical type; in the representatives of this type the dynamic balance is mostly shifted toward a predominance of cortical activity over the subcortical processes. The infracortical centers are hypo-excitable and easily exhaustible, whereas the cerebral cortex develops quite normal activity. All the unconditioned motor, secretory and emotional reactions are diminished. The children show small unconditioned salivation and poor motor activity. They do not like games and sport, but prefer to be alone. The conditioned reflexes are established quickly, but their magnitude does not attain the high level that is characteristic of children of the central type. The decreased unconditioned activity does not represent a favorable basis for the development of intense cortical reactions. The inhibitory conditioned reflexes are formed quickly, but all the inhibitory reactions have the tendency to go over easily into sleep. In later life these persons develop into cool (*temperamentlose*), theoretical intellectualists without strong instincts and emotions. They are not enthusiasts, and their mental activity, although intrinsically correct, is not colored with that individual, vivid expression which is of such great importance for true creative work.

The fourth, anergic or hypodynamic type comprises those in whom both the cerebral cortex and the subcortical regions are equally hypo-excitable. In these children poor mental activity is combined with a decrease of the whole instinctive and unconditioned emotional life. The conditioning of the external situations proceeds here more slowly,

and the intensity of the cortical reflex effects is less than in children of the central type. The conditioned reflex systems are more primitive in structure and show decreased retention and fixation time. The decreased excitability of the cerebral hemispheres is expressed in the form of more or less persistent hypnotic phases (leveling inhibitory, narcotic, paradoxical phases). The children are easily fatigued and cease to respond to stimulations as soon as the latter become more intense or prolonged. Generalized irradiations, especially of an inhibitory process, and decreased concentration and induction are the characteristic features of the cerebral dynamics in these children. In the same fashion the unconditioned reflexes are also weak; hyposecretion and hypokinesis characterize the activity of the extracortical nervous system. This type represents a direct transition to such pathologic conditions as hysteria or, in further development, schizophrenia, in which mental dulness as well as conditional and unconditional emotional dulness are combined in the most hopeless way.

The physiologic method opens an unbounded field for investigation of functional cortical disorders in children, and establishes the fundamental criteria for their prevention and treatment.

One of the most important causes of the cortical neuroses is fatigue or exhaustion of the cortical cells. As soon as some reflex is repeated too often or if the conditioned stimulation lasts too long, the extremely reactive cortical cells become tired and defend themselves by inhibition, ceasing to respond to stimulation. Under these conditions the magnitude of the cortical reflexes progressively decreases, and the reflexes may disappear entirely. For many days and even weeks the stimulation of such cells may produce inhibitory effects, which sometimes influence the reactivity of the whole cerebral cortex.

Another fundamental cause of cortical neuroses is the conflict between excitatory and inhibitory processes. The conflict arises when the child has to inhibit quickly some intense conditioned or unconditioned activities, or when he is forced to pass suddenly from profound inhibition to intense excitement. The functional cortical disturbances develop when children have to solve some difficult inhibitory task, as, for instance, in the establishment of subtle differentiations, in greatly delayed reflexes and in conditioned inhibitions of the intense subcortical reflexes.

The physiology of conflicts and the conditions under which they arise must be well known not only to the physician, but also to all who participate in the education of children. By the careless development of inhibitions and incorrect appraisal of the intensity of the excitations that are to be inhibited, one always risks the production of dynamic disturbances of varying depth and duration, depending on the individual properties of the child's nervous system.

The third fundamental factor producing functional cortical disorders is the action of intense, hypermaximal stimulation. The powerful stimuli producing intense excitation in some cortical fields at the same time inhibit the remainder of the cortex. The state of segregation of the cortex arises, in which the extremely excited cortical cells function autonomically, being beyond the influence of the cortex as a whole. Under these conditions extraordinary stable reflex connections may establish themselves, which thereafter cannot be extinguished by the usual measures, and may persist sometimes for months or even years. For instance, for two years a defective child showed an intense defensive conditioned reflex to the sound of a bell; this had coincided only six times with electric stimulation of the skin and was never reenforced again. The stable autonomic reflexes are easily established in children with an unstable nervous system, e. g., in hysterical patients, in whom the cerebral cortex is especially inclined toward segregation.

The character of the disorders evoked by the factors mentioned is largely determined by the type of nervous system. Some children react with pathologic symptoms of excitation; others show chiefly inhibitory symptoms. The neurosis may either be of a general character or remain strictly localized. Further, there are children in whom the normal reactivity of the cortex is quickly restored, while in others the dynamic disturbance may persist for weeks or even months.

Successful prevention and treatment of functional cortical disorders are impossible unless the factors producing the disturbance are known. A thorough investigation of the environmental conditions and history of the patient usually reveals the necessary data. The second, still more intricate task is to disclose the pathologic dynamic changes in the activity of the cerebral hemispheres, producing abnormal conditions. Careful examination of the cortical functions by means of conditioned reflex tests may give a satisfactory result. By removing the extraneous causes of neurosis and creating favorable conditions for the disturbed cortical function one can, in many cases, effectively better the condition of the patient.

I hope that I have shown that the pediatricians of today are able to investigate the activity of the brain of a child by strictly physiologic methods. A series of physiologic reactions and tests makes possible the examination of the positive and inhibitory activity of the cerebral hemispheres in normal and pathologic children. An unlimited field for further investigation is opened, and I believe that the physiology of a child's brain will find wide development in the United States, where so much attention is paid to children and where pediatrics and biology have made such great progress.

ACID-BASE BALANCE OF NEW-BORN INFANTS

IV. EFFECT OF INGESTION OF ALKALI ON ACID-BASE BALANCE OF NEW-BORN INFANTS

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Previous investigations in this series have presented normal standards for the principal acid and base constituents of the blood serum during the neonatal period. The new-born infant was shown to have a lower carbon dioxide content and a higher chloride content in the serum than the normal adult.[1]

It was subsequently noted that this mild, compensated acidosis was of the metabolic type and dependent on an accumulation of chloride in the blood, possibly associated with inability of the kidneys to excrete chloride during the period of partial dehydration.[2]

More recent studies have shown that the addition of cow's milk to the diet of the new-born infant leads to a fall in the carbon dioxide content of the serum, accompanied by a decrease in serum p_H.[3] Other workers have studied the effect of changes in the electrolyte intake of similar magnitude in adults, older children, infants and animals and have found little or no effect on the acid-base balance, but studies of the new-born infant are not available.

A convenient approach to the subject lies in the study of acid and base ingestion. Investigations in this field have been of considerable value in augmenting our understanding of the fundamental processes involved in the body's regulation of the serum electrolytes.

The ingestion of sufficient quantities of an alkaline salt, such as sodium bicarbonate, produces an increase in the carbon dioxide content of the serum and the alveolar air, an increase in serum p_H and an

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1. Hoag, L. A., and Kiser, W. H.: Acid-Base Equilibrium of New-Born Infants: I. Normal Standards, Am. J. Dis. Child. **41**:1054 (May) 1931.

2. Marples, E., and Lippard, V. W.: Acid-Base Balance of New-Born Infants: II. A Consideration of the Low Alkaline Reserve of Normal New-Born Infants, Am. J. Dis. Child. **44**:31 (July) 1932.

3. Marples, E., and Lippard, V. W.: The Acid-Base Balance of New-Born Infants: III. The Influence of Cow's Milk on the Acid-Base Balance of the Blood of New-Born Infants, Am. J. Dis. Child. **45**:294 (Feb.) 1933.

increase in body weight associated with storage of water and fixed base. Subsequently, the reaction of the urine becomes alkaline, and excretion of ammonia is decreased and replaced by excretion of fixed base bound to chlorides, alkaline phosphates and carbonates until the normal levels are reestablished.[4]

The paucity of available data on the effect of the ingestion of alkalis on the acid-base status of the blood serum of new-born infants prompted this investigation. It is concerned specifically with the following problems:

1. Whether the addition of small amounts of alkali to the new-born infant's diet would produce demonstrable changes in the acid-base status of the blood.

2. Whether the response of older infants to the ingestion of alkalis in comparable amounts would be similar to that of new-born infants.

3. Whether there is an approximately minimum amount of ingested alkali which will balance the acid-producing effect of cow's milk.

SUBJECTS AND METHODS

The subjects selected for this investigation were divided into two groups: first, thirty new-born infants from the nurseries of the New York Nursery and Child's Hospital and, second, fifteen normal older infants who had been admitted to the wards for observation before being placed in foster homes.

The group of new-born infants was similar to that used in previous studies of this series.[5] The infants were all healthy and clinically free from signs of dehydration. Those who had vomited or had fever, excessive loss of weight or cyanotic attacks were excluded. In most instances, observations were begun following the initial period of loss of weight, when the infants were gaining weight. The selection of infants was further limited to those who were receiving formulas exclusively or in part so as to provide a vehicle for the base added.

Preceding observations, the routine feeding schedule of the hospital was invariably followed. The infant was nursed at intervals of six, four and three hours on the first, second and succeeding days, respectively, and received, in addition, about 1 ounce (28.3 Gm.) of a 5 per cent solution of dextrose between feedings.

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4. (*a*) Palmer, W. W., and Van Slyke, D. D.: Studies in Acidosis: IX. Relationship Between Alkali Retention and Alkali Reserve in Normal and Pathological Individuals, J. Biol. Chem. **32**:499, 1917. (*b*) Davies, W. H.; Haldane, J. B. S., and Kennaway, E.: Experiments on the Regulation of the Blood's Alkalinity, J. Physiol. **54**:32, 1920. (*c*) Koehler, A. E.: The Effect of Acid and Base Ingestion Upon the Acid-Base Balance, J. Biol. Chem. **72**:99, 1927.

5. Hoag and Kiser (footnote 1). Marples and Lippard (footnotes 2 and 3).

The first specimen of blood was withdrawn for analysis after the subject had been breast fed in the routine manner for an average of five and one-half days. A mixture of approximately two-thirds cow's milk, one-third water and 5 per cent added carbohydrate in the form of cane sugar was then prescribed as a complementary feeding. To the twenty-four hour formula was added a calculated amount of either sodium bicarbonate or sodium citrate, a uniform distribution of alkali ingestion thus being insured throughout the day.

After a period averaging three and four-tenths days, a second specimen of blood was collected, and the effect of the added electrolyte on the acid-base balance was noted.

Similar studies were made on a group of older infants, varying in age between 2 and 14 months and averaging 6.5 months. These infants were free from infection and malnutrition, and were healthy in all respects.

Their diets remained constant during a control period of several days. At the end of that time, the first specimen of blood was obtained for analysis. Amounts of sodium bicarbonate comparable on the basis of body weight to the amounts given the new-born infants (whose average weight was considered to be 7 pounds [3,182 Gm.]) were then added to their formulas daily for periods of from two to four days. Second specimens of blood were then analyzed.

Blood was obtained by puncture of either the external or the internal jugular veins and at once immersed in paraffin oil. All collections were made about two hours after the last feeding. Analyses were started within an hour of the time of collection. In these and all other respects, the technic of collection and analysis was the same as that used in the previous investigations of this series.[5]

RESULTS

Effect of the Ingestion of Sodium Bicarbonate on New-Born Infants.—A group of seventeen new-born infants was given sodium bicarbonate in daily dosages varying between 1 and 0.125 Gm.

The results are shown in table 1. In considering them, it must be remembered that the ingestion of cow's milk by new-born infants produces a diminution in the carbon dioxide content of the blood.[8] The values for that factor obtained in the second analyses, therefore, represent the resultants of two forces, i. e., the tendency of cow's milk to decrease and that of sodium bicarbonate to increase the carbon dioxide content.

In this group and in those following, occasional cases do not conform in one or more respects to the general average. Individual analyses in different infants vary, although daily analyses on the same

TABLE 1.—*Effect of the Ingestion of Sodium Bicarbonate on the Acid-Base Balance of the Serum of New-Born Infants* *

Case	Birth Weight, Gm.	Age, Days	Weight, Gm.	Daily Intake of Sodium Carbonate, Gm.	p_H	Carbon Dioxide Content, Volume per Cent	$BHCO_3$, mM.	Carbon Dioxide Tension, Mm.	Sodium Chloride		Protein		Total Acid Determined, mM.	Undetermined Acid, mM.	Total Fixed Base, mM.
									Mg. per 100 Cc.	mM.	Per Cent	mM.			
A. EFFECT OF THE DAILY INGESTION OF 1.0 GM. SODIUM BICARBONATE															
81	3,911	9	3,685	1.0	7.43	50.8	21.7	33.8	...	.....	5.20	13.0	.....	....	149.9
		11	3,771		7.38	50.3	21.3	37.3	621	106.3	5.17	13.0	140.6	9.3	149.9
82	3,317	5	3,005	1.0	....	43.1	18.5	23.5	639	109.3	7.28	19.4	147.2	10.3	157.5
		8	3,317		7.49	58.3	25.0	34.0	604	103.3	6.28	16.5	144.8	....	.....
83	3,175	6	2,949	1.0	7.40	45.1	19.2	32.1	665	113.7	6.89	17.4	150.3	5.0	155.3
		10	3,146		7.48	58.9	25.2	35.1	600	102.6	5.72	15.0	142.8	1.4	144.2
84	2,892	8	2,778	1.0	7.37	50.3	21.3	38.1	633	108.3	6.51	16.3	145.9	4.9	150.8
		10	2,863		7.38	56.5	24.0	41.9	601	102.9	5.81	14.6	141.5	5.7	147.2
86	3,629	4	3,303	1.0	7.40	59.3	25.2	42.1	616	105.4	6.48	16.4	147.0	...	143.2
		9	3,430		7.52	63.3	27.2	34.5	576	98.5	5.59	14.9	140.6	5.5	146.1
87	3,260	7	3,002	1.0	7.41	53.6	22.8	37.2	616	105.4	6.31	16.0	144.2	8.1	152.3
		11	3,090		7.47	59.1	25.3	36.0	609	104.2	5.21	13.6	143.1	1.6	144.7
Average	3,365	6.5	3,130		7.40	50.4	21.5	34.5	634	108.4	6.45	16.4	146.9	4.6	151.5
		10	3,270		7.46	57.7	24.7	36.5	602	103.0	5.63	14.6	142.2	4.2	146.4
B. EFFECT OF THE DAILY INGESTION OF 0.5 GM. SODIUM BICARBONATE															
89	3,969	5	3,685	0.5	7.40	51.6	21.9	36.7	594	101.6	5.14	13.0	136.5	12.4	148.9
		8	4,025		7.40	60.5	25.7	43.0	588	100.6	5.24	13.3	139.5	9.1	148.7
92	3,685	7	3,496	0.5	7.38	50.3	21.4	37.3	597	102.1	5.56	13.9	137.4	10.8	148.2
		10	3,571		7.40	55.9	23.8	39.7	598	102.4	6.41	16.2	142.4	....	141.3

96	3,714	4	3,515	0.5	7.42	47.9	20.4	32.5	622	106.4	5.91	15.1	141.9	11.3	153.2
		7	3,685		7.44	63.6	27.1	41.3	605	103.5	5.46	14.1	144.7	....	143.1
97	3,657	3	3,496	0.5	7.42	58.0	24.7	39.4	620	106.1	6.07	15.5	146.3	4.6	150.9
		7	3,543		7.42	52.0	22.2	35.4	616	105.4	5.45	13.9	141.5	4.7	149.1
98	3,515	5	3,288	0.5	7.43	52.7	22.5	35.0	633	108.3	5.14	13.2	144.0	16.2	160.2
		8	3,463		7.43	56.3	24.0	37.5	628	107.4	5.07	13.0	144.4	8.1	152.5
Average	3,708	4.8	3,496		7.41	52.1	22.2	36.2	613	104.9	5.56	14.1	141.2	11.1	152.3
		8.0	3,657		7.42	57.7	24.6	39.4	607	103.9	5.53	14.1	142.6	4.3	146.9
C. EFFECT OF THE DAILY INGESTION OF FROM 0.125 to 0.25 GM. SODIUM BICARBONATE															
94	4,054	3	3,657	0.25	7.42	48.4	20.6	32.9	654	111.8	6.26	16.0	148.4	....	.....
		7	3,827		7.40	48.1	20.5	34.2	631	107.9	5.50	13.9	142.3	2.7	145.0
95	3,799	4	3,496	0.25	7.33	42.0	17.7	34.7	651	111.4	7.71	18.9	148.0	2.6	150.6
		8	3,601		7.36	52.3	22.1	40.5	623	106.5	5.73	14.4	143.0	2.9	145.9
110	3,571	7	3,430	0.25	7.42	54.9	23.4	37.3	596	102.0	5.71	14.6	140.0	....	.....
		9	3,477		....	59.4	25.5	32.4	609	104.1	5.49	14.6	144.2	5.1	149.3
111	3,373	6	3,005	0.25	7.42	62.4	26.6	41.5	647	110.7	5.79	14.8	152.1	8.8	161.9
		8	3,175		7.43	56.6	24.2	37.7	625	107.0	5.67	14.5	145.7	2.7	148.4
93	3,940	7	3,855	0.125	7.42	52.0	22.2	35.3	603	103.1	5.79	14.8	140.1	5.0	146.1
		10	3,883		7.43	51.1	21.8	34.0	596	101.9	6.08	15.6	139.3	6.4	145.7
109	4,365	3	3,969	0.125	7.43	50.7	21.6	33.7	666	114.0	6.20	15.9	151.5	5.9	157.4
		6	4,247		7.38	51.3	21.8	38.0	634	108.5	5.67	14.2	144.5	....	.....
Average	3,850	5	3,569		7.41	51.7	22.0	35.9	636	108.8	6.24	15.8	146.7	7.3	154.0
		8	3,702		7.40	53.1	22.7	36.1	620	106.0	5.69	14.5	143.2	3.7	146.9

* The data in the first line in each case were recorded at the end of a period of breast milk feeding, while those in the second line indicate the changes which resulted from the administration of cow's milk plus the stated amount of sodium bicarbonate during the interval noted.

infant during this age period have been found to be fairly constant.[3] Taking these observations into consideration, the results are surprisingly consistent.

A daily dosage of 1 Gm. of sodium bicarbonate was arbitrarily chosen for group A. Determinations on six infants revealed decided elevations in the serum carbon dioxide contents, averaging 7.3 per cent by volume, and moderate elevations in serum p_H following the ingestion of alkali. Decreases in serum chloride, protein, total determined acid and fixed base were also of sufficient magnitude to be significant.

Less pronounced, but still definite, changes were observed in group B, in which the daily dosage of sodium bicarbonate was decreased to 0.5 Gm. The average elevation of the carbon dioxide content was found to be 5.6 per cent by volume. Other observations paralleled those of the previous group, but were of less magnitude. The comparatively large difference in values for unanalyzed acid found in this group does not conform to the results found in other groups and must be considered a technical error.

In group C, the dosage of alkali was decreased to 0.25 Gm. and in two cases to 0.125 Gm. per day. Examination of the table will reveal the fact that alterations resulting from the larger dosage are variable and probably indicate a borderline effect. The daily ingestion of 0.125 Gm. of sodium bicarbonate (cases 93 and 109) produced changes which are not sufficiently great in either direction to be considered significant.

The data suggest that the daily ingestion of sodium bicarbonate within a minimum range of 0.125 and 0.25 Gm. is capable of compensating for the acid-producing effect of cow's milk in the new-born infant. It appears safe to postulate that the effect of ingested alkali, even in these minimal amounts, would still be evident in the absence of the interfering factor of the ingestion of cow's milk.

A review of the whole series reveals the following significant facts:

1. Remarkable changes in p_H were noted only in the group receiving 1 Gm.

2. Values for serum bicarbonate and carbon dioxide tension showed gradually diminishing changes in direct proportion to the amount of ingested alkali.

3. Marked diminution in serum chloride was observed in the group receiving 1 Gm. and slight decreases in the groups receiving smaller amounts.

4. Serum protein concentration was definitely decreased in those receiving 1 Gm. and to a lesser extent in those receiving smaller amounts.

5. Both total determined acid and total fixed base were slightly diminished in all groups. (The influence of serum dilution on these values is discussed later).

The Effect of the Ingestion of Sodium Citrate on New-Born Infants.—If alkalosis from sodium bicarbonate is to be ascribable to base retention, other sodium salts with easily metabolizable acid radicals should have the same effect. Sodium citrate, which resembles sodium bicarbonate in that it is a sodium salt of a weak organic acid, was administered in daily doses of 1.17 Gm., each of which had a sodium content equivalent to that of 1 Gm. of sodium bicarbonate. The salt has the theoretical advantage of not acting as an alkali in the alimentary canal, of being less nauseating and of not causing gaseous eructations.[6]

The effect of the daily ingestion of 1.17 Gm. of sodium citrate on the acid-base balance of the blood of thirteen new-born infants is shown in table 2. The trend of the alterations is essentially the same as that previously noted for an equivalent dosage of sodium bicarbonate. The average increase in p_H and serum bicarbonate corresponds closely in the two groups. The average diminution in serum chloride, protein, total determined acid and total fixed base, however, is somewhat less marked. We are not at present able to account for this variation, although it has been suggested that the absorption of the salt and the oxidation of the citrate radical may have been less complete than in the case of bicarbonate.

The Effect of the Ingestion of Sodium Bicarbonate on Older Infants —Aged 2 to 14 Months.—Having established the minimum amount of sodium bicarbonate necessary to affect the acid-base balance of the blood of infants during the first ten days of life, our next step was to determine the effect of equivalent doses on a group of older infants. Assuming the average weight of the new-born infants previously studied to be about 3,182 Gm. (7 pounds), amounts of sodium bicarbonate proportional by weight to the effective doses for new-born infants were given to the older group.

Two 3 month old infants were given doses of 0.5 Gm. per 3,182 Gm. of body weight daily without effect on the acid-base balance. The amount was therefore increased to 1 Gm. per 3,182 Gm. of body weight per day.

The effect of the ingestion of that dose on a group of ten infants is shown in the first part of table 3. It may be readily seen that the results of the first and second analyses are not appreciably different.

6. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1, p. 973.

TABLE 2.—*Effect of the Ingestion of Sodium Citrate on the Acid-Base Balance of the Serum of New-Born Infants* *

Case	Birth Weight, Gm.	Age, Days	Weight, Gm.	Daily Intake of Sodium Citrate, Gm.	p_H	Carbon Dioxide Content, Volume per Cent	$BHCO_3$, mM.	Carbon Dioxide Tension, Mm.	Sodium Chloride		Protein		Total Acid Determined, mM.	Undetermined Acid, mM.	Total Fixed Base, mM.
									Mg. per 100 Cc.	mM.	Per Cent	mM.			
150†	3,373	7	3,232	1.17	7.41	55.2	23.5	38.3	634	108.5	5.96	15.1	147.1	....	146.3
		12	3,430		7.48	65.5	28.1	39.0	619	105.8	5.34	14.0	147.9	2.0	149.9
151	3,515	7	3,274	1.17	7.43	54.4	23.2	36.3	636	108.8	5.80	14.9	146.9	3.9	150.8
		10	3,288		7.48	56.8	24.4	33.8	616	105.3	5.54	14.5	144.2	9.6	153.8
152	3,855	1	3,808	1.17	7.42	54.3	23.1	36.9	546	93.5	6.12	15.6	132.2	8.2	140.4
		4	3,685		7.46	54.8	23.4	34.1	551	94.3	5.59	14.5	132.2	10.0	142.2
153	3,799	9	3,733	1.17	7.42	52.6	22.4	35.8	609	104.1	5.96	15.2	141.7	12.1	153.8
		13	3,855		7.49	57.7	24.7	33.6	...	.....	5.38	14.1	.....	....	141.1
154	3,515	7	3,416	1.17	7.42	52.8	22.5	35.9	629	107.6	5.36	13.7	143.8	5.1	148.9
		10	3,515		7.51	63.2	27.2	35.2	619	105.8	4.82	12.8	145.8	7.5	153.3
155	3,855	7	3,685	1.17	7.46	63.2	27.0	39.3	615	105.1	5.30	13.7	145.8	3.1	148.9
		10	3,911		7.42	56.0	23.9	38.1	600	102.7	5.30	13.5	140.1	10.9	151.0
156	4,307	6	4,025	1.17	7.42	42.7	18.2	29.1	609	104.2	5.74	14.6	137.0	12.1	149.1
		10	4,307		7.45	55.7	23.8	35.4	606	103.7	4.96	12.8	140.3	9.3	149.6
157	3,940	3	3,343	1.17	7.43	50.6	21.6	33.7	664	113.5	5.71	14.6	149.7	7.2	156.9
		6	3,799		7.37	49.1	20.8	37.2	650	111.2	4.80	12.0	144.0	7.6	151.6
158	3,000	4	2,863	1.17	7.39	51.8	21.9	37.5	617	105.5	5.46	13.8	141.2	4.8	146.0
		7	2,977		7.44	59.8	25.5	38.9	628	107.3	4.91	12.6	145.4	7.2	152.6
159	2,949	3	2,722	1.17	7.38	41.0	17.4	30.4	615	105.3	5.91	14.8	137.5	13.9	151.4
		6	2,927		7.44	58.2	24.8	37.8	623	106.6	4.52	11.6	143.0	5.8	148.8
160	2,802	7	2,920	1.17	7.43	60.9	26.0	40.5	635	108.6	5.04	12.9	147.5	4.2	151.7
		10	3,000		7.44	64.1	27.4	41.7	602	103.0	4.87	12.5	142.9	6.8	149.7
161	3,402	6	3,218	1.17	7.44	56.6	24.2	36.8	597	102.1	4.90	12.6	138.9	4.4	143.3
		10	3,402		7.47	69.7	29.8	42.4	572	97.9	5.53	14.4	142.1	....	140.3
162	3,940	8	3,799	1.17	7.42	56.7	24.2	38.6	631	108.0	5.32	13.6	145.8	4.4	150.2
		12	3,911		7.47	56.2	24.1	34.2	607	103.8	5.81	15.1	143.0	7.7	150.7
Average	3,572	5.8	3,388		7.42	53.3	22.7	36.1	618	105.7	5.58	14.2	142.6	6.5	149.1
		9.2	3,546		7.46	59.0	25.2	37.0	608	104.0	5.18	13.4	142.6	6.2	148.8

* The data in the first line in each case were recorded at the end of a period of breast milk feeding, while those in the second line indicate the changes which resulted from the administration of cow's milk plus the stated amount of sodium citrate during the interval noted.

† Infant received sodium citrate from the ninth to twelfth days inclusive.

Another group of five infants was then given daily doses of 1.5 Gm. of sodium bicarbonate per 3,182 Gm. of body weight. On this dosage, changes in serum p_H were not remarkable, but the serum bicarbonate showed a definite increase in all cases (7.1 per cent by volume carbon dioxide content). The serum protein underwent a slight decrease, while the serum chloride, the total determined acid and the total fixed base remained essentially unaltered.

A comparison of the results obtained in the older and the new-born groups of infants shows that the minimum dosage of sodium bicarbonate effective in disturbing the acid-base balance of the blood of older infants notably exceeds the minimum dosage effective for new-born infants. This evidence seems adequate to support the theory of an accentuated lability of the acid-base mechanism in the neonatal period.

The Effect of the Ingestion of Alkaline Salts on the Weight Curves of New-Born Infants—Many investigators have realized that there is a relationship between the base and water content of the organism. On this theory are based numerous experiments by Gamble and his associates regarding the effect of acid and alkali on the elimination and retention of water in normal persons and those with kidney dysfunctions.[7] It appears to be firmly established that "retention of base entails retention of water and accumulation of water is associated with storage of base."[8]

This theory has been applied in feeding experiments on breast-fed new-born infants by Eder and Bakewell.[9] Although no metabolic studies were conducted, they found clinically that the initial loss in weight was diminished and birth weight regained more rapidly following the daily ingestion of 2 Gm. of sodium citrate.

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7. Gamble, J. L., and Ross, G. S.: Studies of Tetany: II. The Effect of Ingestion of Hydrochloric Acid Producing Substances on the Acid-Base Metabolism of an Infant and the Probable Manner of Their Action in the Treatment of Tetany, Am. J. Dis. Child. **25**:470 (June) 1923. Gamble, J. L.; Blackfan, K. D., and Hamilton, B.: A Study of the Diuretic Action of Acid-Producing Salts, J. Clin. Investigation **1**:359, 1925. Gamble, J. L.; Ross, S. G., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, J. Biol. Chem. **57**:633, 1923. Gamble, J. L., and McIver, M. A.: A Study of the Effects of Pyloric Obstruction in Rabbits, J. Clin. Investigation **1**:531, 1925. Gamble, J. L., and Ross, S. G.: The Factors in the Dehydration Following Pyloric Obstruction, J. Clin. Investigation **1**:403, 1925. Gamble, J. L.; Ross, S. G., and Tisdall, F. F.: Studies of Tetany: I. The Effect of Calcium Chloride Ingestion on the Acid-Base Metabolism of Infants, Am. J. Dis. Child. **25**:455 (June) 1923.

8. Peters and Van Slyke (footnote 6, p. 761).

9. Eder, H. L., and Bakewell, B.: Effect of Sodium Citrate on the Loss of Weight in the New-Born Infant, Am. J. Dis. Child. **42**:1079 (Nov.) 1931.

TABLE 3.—*Effect of the Ingestion of Sodium Bicarbonate on the Acid-Base Balance of the Serum of Infants, Aged 2 to 14 Months* *

Case	Age, Months	Weight, Kg.	Interval Between First and Second Blood Analyses, Days	Daily Dosage of Sodium Bicarbonate Gm. per 3,182 Gm. Body Weight	p_H	Carbon Dioxide Content, Volume per Cent	$BHCO_3$, mM.	Carbon Dioxide Tension, Mm.	Sodium Chloride		Protein		Total Acid Determined, mM.	Undetermined Acid, mM.	Total Fixed Base, mM.
									Mg. per 100 Cc.	mM.	Per Cent	mM.			
A. EFFECT OF THE DAILY INGESTION OF 1.0 GM. SODIUM BICARBONATE PER 3,182 GM. BODY WEIGHT															
200	2	3.36	2	1.0	7.38	55.1	23.4	40.9	594	101.5	5.86	14.7	139.6	11.3	150.9
					7.40	55.0	23.4	39.1	587	100.4	5.64	14.3	138.1	10.5	148.6
201	5	6.93	2	1.0	7.34	51.5	21.7	41.7	590	100.9	6.48	16.0	138.6	3.8	142.4
					7.34	54.1	22.8	43.9	584	99.9	6.19	15.3	138.0	4.3	142.3
202	6	6.80	2	1.0	7.38	51.8	22.0	38.4	600	102.7	6.17	15.5	140.2	3.2	143.4
					7.38	53.4	22.7	39.6	592	101.3	6.32	15.9	139.9	7.6	147.5
203	4	4.08	2	1.0	7.41	51.1	21.7	35.5	592	101.2	5.93	15.1	138.0	7.0	145.0
					7.39	59.7	25.3	43.3	571	97.8	5.86	14.8	137.9	5.7	143.6
204	6.5	6.66	3	1.0	7.42	52.9	22.6	36.0	600	102.7	6.47	16.5	141.8	5.0	146.8
					7.39	51.4	21.8	37.3	615	105.2	6.56	16.5	143.5	1.3	144.8
205	3.5	4.27	4	1.0	7.43	55.7	23.8	37.0	589	100.7	5.55	14.2	138.7	6.6	145.3
					7.42	57.8	24.6	39.3	579	99.0	5.93	15.1	138.7	8.3	147.0
206	10	6.80	4	1.0	7.33	50.6	21.3	41.8	599	102.5	6.63	16.3	140.1	8.7	148.8
					7.47	56.6	24.2	34.4	590	100.9	5.99	15.6	140.7	2.4	143.1
207	5	4.99	2	1.0	7.43	52.4	22.3	34.8	594	101.7	5.84	15.0	139.0	7.4	146.4
					7.38	51.3	21.8	38.1	588	100.5	6.43	16.1	138.4	10.2	148.6
208	4	4.54	3	1.0	7.38	48.9	20.7	36.2	633	108.4	5.57	14.0	143.1	10.7	153.8
					7.43	49.1	20.9	32.6	613	104.8	5.67	14.5	140.2	7.0	147.2
209	14	11.34	2	1.0	7.40	54.0	23.0	38.4	609	104.1	6.64	16.8	143.9	6.8	150.7
					7.41	56.2	23.9	39.0	631	107.9	6.22	15.8	147.6	6.6	154.2
Average	6	5.98	2.6	1.0	7.39	52.4	22.3	38.1	600	102.6	6.11	15.4	140.3	7.1	147.4
					7.40	54.5	23.1	38.7	595	101.8	6.08	15.4	140.3	6.4	146.7
B. EFFECT OF THE DAILY INGESTION OF 1.5 GM. SODIUM BICARBONATE PER 3,182 GM. BODY WEIGHT															
213	7	5.46	3	1.5	7.39	54.8	23.3	39.8	608	104.0	6.51	16.4	143.7	5.2	148.9
					7.39	61.3	26.0	44.5	601	102.9	6.02	15.2	144.1	2.9	147.0
214	7	5.44	3	1.5	7.36	48.1	20.4	37.3	620	106.0	6.79	16.9	143.3	8.3	151.6
					7.34	57.8	24.4	46.8	605	103.4	6.53	16.1	143.9	0.3	144.2
215	8	5.24	3	1.5	7.41	52.3	22.2	36.3	613	104.8	6.08	15.4	142.4	5.3	147.7
					7.40	63.8	27.1	45.4	603	103.1	5.75	14.5	144.7	2.0	146.7
216	8	8.15	3	1.5	7.42	49.7	21.2	33.8	622	106.5	6.26	16.0	143.7	8.6	152.3
					7.49	55.8	23.9	32.5	608	103.9	6.28	16.5	144.3	3.2	147.5
217	8	5.78	3	1.5	7.42	59.8	25.5	40.7	599	102.6	6.68	17.0	145.1	....	145.1
					7.44	61.6	26.3	40.1	597	102.2	6.06	15.6	144.1	2.1	146.2
Average	7.6	6.01	3	1.5	7.40	52.9	22.5	37.6	612	104.8	6.46	16.3	143.6	5.5	149.1
					7.41	60.0	25.5	41.9	603	103.1	6.13	15.6	144.2	2.1	146.3

* The data in the first line in each case were recorded at the end of a control period, while those in the second line indicate the changes which resulted from the daily administration of the stated amount of sodium bicarbonate during the interval noted.

The changes in weight in a series of new-born infants who were fed cow's milk formulas plus sodium bicarbonate and sodium citrate and the average changes which occurred in a control group of about one hundred and fifty infants who were given only cow's milk formulas

TABLE 4.—*Effect of the Daily Ingestion of Sodium Bicarbonate and Sodium Citrate on the Body Weight of New-Born Infants*

Case	Day of Life		Gain in Absolute Weight, Gm.		Gain in Percentage of Birth Weight	
	Before Ingestion	After Ingestion	Average in Control Group	Infants Receiving Alkali	Average in Control Group	Infants Receiving Alkali
A. Effect of Daily Ingestion of 1 Gm. Sodium Bicarbonate						
81	9	11	18	86	0.6	2.2
82	5	8	99	312	3.0	9.4
83	6	10	163	197	4.6	6.2
84	8	10	61	85	1.8	2.9
86	4	9	158	122	4.6	3.4
87	7	11	100	28	3.2	0.9
Average			99.8	155	2.97	4.16
B. Effect of Daily Ingestion of 0.5 Gm. Sodium Bicarbonate						
89	5	8	99	340	3.0	8.6
92	7	10	89	75	2.9	2.0
96	4	7	120	170	3.5	4.6
97	3	7	155	47	4.7	1.3
98	5	8	99	175	3.0	5.0
Average			112.4	161.4	3.42	4.30
C. Effect of Daily Ingestion of from 0.125 to 0.25 Gm. Sodium Bicarbonate						
93	7	10	89	28	2.9	0.7
94	3	7	155	170	4.7	4.2
95	4	8	150	105	4.4	2.8
109	3	6	147	278	4.4	6.4
111	6	8	73	170	2.1	5.0
110	7	9	64	47	2.0	1.3
Average			113	133	3.40	3.40
D. Effect of Daily Ingestion of 1.17 Gm. Sodium Citrate						
150	7	12	120	198	3.8	5.9
151	7	10	89	14	2.9	0.4
152	1	4	−48	−123	−1.6	−3.2
153	9	13	100	122	3.1	3.2
154	7	10	89	99	2.9	2.8
155	7	10	89	226	2.9	5.9
157	3	6	147	256	4.4	6.4
156	6	10	163	282	4.6	6.5
158	4	7	120	114	3.5	3.7
159	3	6	147	205	4.4	7.0
160	7	10	89	170	2.9	5.9
161	6	10	163	184	4.6	5.4
162	8	12	121	112	3.6	2.8
Average			106.8	143	3.23	4.05

over similar age periods have been tabulated. All infants considered were in the same institution and fed under identical conditions.

The alteration in weight in each case is compared with the average change in absolute weight and percentage of weight at birth in the members of the control group in which cow's milk formulas were started on the same day of life and continued for a similar number of days. A larger number of controls might have been selected for comparison if published data had been used in which the character and date of onset

The data in the first line in each case were recorded at the end of a control period, while those in the second line indicate the changes which resulted from the daily administration of the stated amount of sodium bicarbonate during the interval noted.

of artificial feeding were not considered. Comparison with a group like the one described seems more valid.

The results are shown in table 4. It may be readily seen that the absolute as well as the percentage gain in weight was greater in the group of infants who received the alkaline salt in addition to the routine formula than it was in the control groups. The alteration in percentage of birth weight is perhaps a more legitimate standard of comparison than the absolute change in grams, since a large infant is more likely to show greater fluctuation during this age period than a small one.

The number of cases under consideration does not permit comparison between groups receiving various amounts of sodium bicarbonate and citrate.

COMMENT

It is interesting to speculate on the diverse effects of comparable doses of alkali on the new-born and older infant. The minimum effective dose of sodium bicarbonate for the new-born infant, whose average weight was considered for purposes of comparison to be 3,182 Gm. (7 pounds), was found to be between 0.125 and 0.25 Gm. per day, yet the acid-base balance of the blood of older infants was not altered until daily doses of 1.5 Gm. per 3,182 Gm. of body weight were administered.

The results obtained in the older infants are essentially in agreement with those of other investigators in adults who were also given comparatively larger doses of alkali than those which were administered to the new-born infants. Differences in the plan of experimentation, such as time distribution of ingestion, prohibit direct comparison.

Palmer and Van Slyke [4a] gave normal adults and patients with nephritis sodium bicarbonate in 2 Gm. doses at frequent intervals in order to determine the relationship between alkali retention and alkali reserve. They found appreciable increases in the combined carbon dioxide of the plasma after a patient had taken 6 Gm. during an interval of one and one-half hours, at which time the urine had reached a p_H of 7.4. The effect of more prolonged administration was not studied. Elaboration of that work was performed by Palmer, Salvesen and Jackson,[10] who determined that the level of the plasma carbon dioxide content at which the first depression effect of the alkali on urinary acidity is noted is 68 ± 10 per cent by volume.

Adults weighing 75 and 97 Kg. were given from 30 to 57 Gm. of sodium bicarbonate in one dose by Davies, Haldane and Kennaway.[4b]

10. Palmer, W. W.; Salvesen, H., and Jackson, H., Jr.: Relationship Between the Plasma Bicarbonate and Urinary Acidity Following the Administration of Sodium Bicarbonate, J. Biol. Chem. **45**:101, 1920.

An increase was noted in the carbon dioxide capacity of the blood, the alveolar carbon dioxide and the concentration of sodium bicarbonate in the urine, as well as a moderate diuresis and decrease in urinary ammonia. Haldane [11] later advocated the use of 45 Gm. of sodium bicarbonate and 70 Gm. of sodium acetate as adequate doses for an adult.

More recently, Koehler [4c] has given adults sodium bicarbonate and sodium citrate in doses of from 20 to 40 Gm. per day for from sixteen to twenty-one days. This prolonged administration resulted in increases in serum p_H from 7.40 to 7.55 and in the serum carbon dioxide content from 50 to 65 per cent by volume. An increase in body weight was also noted in all cases.

Allbright and Bauer [12] gave an adult with nephrosis 21 Gm. (2,500 cc. of tenth-normal) sodium bicarbonate during a period of three days. The serum carbon dioxide content and the fixed base were increased while the serum chloride was diminished. The serum protein was low at the onset of the experiment and was not appreciably altered. During the period of ingestion of alkali, the patient gained weight in the form of edema fluid approximately in proportion to the total base retention.

The effect of the ingestion of alkaline salt on the complete acid-base balance of the blood of infants and children has not been studied previously. Courtney and Fales [13] found low values for plasma chloride following subcutaneous injections of unrecorded amounts of sodium bicarbonate. More recently, Hartmann and Senn [14] determined a quantitative relationship between the amount of injected sodium bicarbonate or sodium lactate and the increase in carbon dioxide content of body water. Shohl and Sato [15] gave a 9 month old infant 3.97 Gm. of sodium bicarbonate during a period of three days and noted an increase in the positive base balance. The effect on the blood serum was not considered.

The data of these authors substantiate the observation that the acid-base balance of the blood undergoes a change in older infants and

11. Haldane, J. B. S.: Experimental and Therapeutic Alterations of Human Tissue Alkalinity, Lancet **1**:537, 1924.

12. Allbright, F., and Bauer, W.: The Action of Sodium Chloride, Ammonium Chloride and Sodium Bicarbonate on the Total Acid-Base Balance of a Case of Chronic Nephritis with Edema, J. Clin. Investigation **7**:465, 1929.

13. Courtney, A. M., and Fales, H. L.: Variations in Infants of Total Blood Solids and the Concentration of Sodium Chloride in the Plasma, Am. J. Dis. Child. **14**:202 (Sept.) 1917.

14. Hartmann, A. F., and Senn, M. J.: Alkali Therapy, Am. J. Dis. Child. **42**:693 (Sept.) 1931.

15. Shohl, A. T., and Sato, A.: Acid-Base Metabolism: I. Determination of Base Balance, J. Biol. Chem. **58**:235 (Sept.) 1923.

adults similar to that in new-born infants, but only under the influence of proportionally larger amounts of alkali.

In older persons, the physiologic regulation seems to be sufficient to compensate for small alterations in the acid-base ratio of the intake so as to prevent their influencing the acid-base balance of the blood. Our results would suggest that during the neonatal period these mechanisms are not capable of performing this function so efficiently. This point, which may very well be the principle underlying the lability of the acid-base mechanism in the new-born, has been stressed, and the literature on the subject thoroughly reviewed in previous communications.[16] Continuation of these investigations led to the study of the

TABLE 5.—*Total Serum Anions Minus Bicarbonate Before and After Ingestion of Alkaline Salts* *

Group	Chloride, mM.	Protein, mM.	Undetermined Acid, mM.	Total, mM.	Difference, mM.
New-born infants receiving 1 Gm. sodium bicarbonate daily (table 1-A).....	108.4 103.0	16.4 14.6	4.6 4.2	129.4 121.8	—7.6
New-born infants receiving 0.5 Gm. sodium bicarbonate daily (table 1-B)..	104.9 103.9	14.1 14.1	11.1 4.3	130.1 122.3	—7.8
New-born infants receiving 0.125-0.25 Gm. sodium bicarbonate daily (table 1-C)	108.8 106.0	15.8 14.5	7.3 3.7	131.9 124.2	—7.7
New-born infants receiving 1.17 Gm. sodium citrate daily (table 2).....	105.7 104.0	14.2 13.4	6.5 6.2	126.4 123.6	—2.8
Older infants receiving 1 Gm. sodium bicarbonate per 7 pounds of body weight daily (table 3-A)	102.6 101.8	15.4 15.4	7.1 6.4	125.1 123.6	—1.5
Older infants receiving 1.5 Gm. sodium bicarbonate per 7 pounds of body weight daily (table 3-B)	104.8 103.1	16.3 15.6	5.5 2.1	126.6 120.8	—5.8

* The data in the first line in each group were recorded at the end of a period of breast milk feeding, while those in the second line indicate the changes which resulted from the administration of cow's milk plus the stated amount of sodium bicarbonate during the intervals noted.

effect of the ingestion of alkaline salts, following which an increase in alkali reserve was demonstrated.

Theoretically, this increase in alkali reserve may have been produced by either one or both of the following mechanisms: a relative decrease in the total anions other than bicarbonate or a relative increase in the total fixed base.

A decrease in total anions minus bicarbonate, that is, total base bound by chloride, protein, phosphate, sulphate and organic acid, was observed in all groups receiving sodium bicarbonate or sodium citrate (table 5). This would suggest that the first mechanism is the one involved.

A relative increase in total fixed base was found to be singularly absent in any of the groups, either of new-born or of older infants. The

16. Marples and Lippard (footnotes 2 and 3).

general tendency, on the other hand, was toward a diminution in that factor after the ingestion of the alkaline salts, a slight decrease having been observed in all groups.

This diminution in total base may be explained by dilution of the plasma. Indexes of alterations in plasma concentration in the body which are considered reliable are the changes that take place in the concentration of serum protein and the specific gravity.[17] An approximately quantitative relationship between the serum protein and the plasma concentration has been recognized for many years and has been of value in studies of dehydration accompanying diarrhea and of inanition fever in the new-born.[18]

All determinations of serum protein were performed under the same experimental conditions. Although the method used is based on refractometric readings and the values obtained are somewhat higher than those obtained by the Kjeldahl method, the comparison of the values before and after alkali ingestion is still valid. This point has been discussed extensively in a previous communication.[2]

It has been previously demonstrated that there is a normal fluctuation in the serum protein concentration during the first few days of life. The alterations noted in this series, however, are of such magnitude and constancy as definitely to establish their significance.

If we may assume that the serum is diluted in proportion to the decrease in serum protein, the diminution in fixed base has been relative, and in reality the total amount of fixed base in the infant's serum is increased. This would serve to substantiate the following hypothesis: The increase in serum bicarbonate observed is balanced by an increase in total fixed base rather than a decrease in other acids, although the increase is not reflected in the serum concentration.

The production of a decrease in the alkali reserve of a group of new-born infants following the ingestion of cow's milk has previously been demonstrated.[3] The average decrease in the carbon dioxide content of the serum observed in sixty-seven infants was approximately 5 per cent by volume. Table 1 C illustrates how this alteration may be compensated by the addition of very small amounts of alkali, equivalent to from 0.125 to 0.25 Gm. of sodium bicarbonate. In that group, the carbon dioxide values after the ingestion of cow's milk plus sodium bicarbonate remained at essentially the same level as they were when the infants were fed breast milk.

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17. Spencer, H.: The Water Content of Blood Serum, Am. J. Dis. Child. **37:** 546 (March) 1929.

18. Bakwin, H., and Goss, C.: Dehydration in New-Borns, Am. J. Dis. Child. **24:**497 (Dec.) 1922; Dehydration Fever in New-Borns, ibid., p. 508.

If this adjustment is beneficial, the addition of small amounts of sodium bicarbonate or sodium citrate to the cow's milk formulas of infants during the neonatal period may be desirable. Other investigators, from entirely different points of view, have come to a similar conclusion, although a record of the results of this type of feeding in a series of infants has not been found.

In a discussion of the value of acid milks in the feeding of older infants, Faber [19] emphasized the observation that the p_H of colostrum is 7.74 as compared with 6.97 in breast milk and 6.7 [20] in cow's milk. He also stated: "This may well point to the desirability of increasing the alkalinity of artificial food during the first month, lowering the buffer resistance to alkaline change, and may offer an explanation for the occasional usefulness of lime water."

Studies of gastric digestion in the new-born by Griswold and Shohl [21] established the fact that their gastric acidity is p_H 2.5 to 2.6 as contrasted with p_H 3.9 to 4.6 in older infants, and that ingested food leaves the stomach more rapidly in the former group. They concluded that it would, therefore, seem logical to feed new-born infants a more concentrated and more alkaline food.

Because conditions frequently arise in the mother which make nursing of the infant impossible, it is often necessary to substitute a cow's milk feeding even during the first few days of life. There may be certain theoretical advantages in feeding new-born infants alkali in conjunction with cow's milk when substitution is imperative. The following factors are worthy of consideration: (*a*) The acid-producing effect of cow's milk may be neutralized. (*b*) The initial loss of weight and dehydration during the first few days of life may be diminished. (*c*) The combination of cow's milk and alkali more nearly approaches the acidity of colostrum and early breast milk than does cow's milk alone. (*d*) The gastric juice of new-born infants is more acid and therefore capable of neutralizing a more alkaline food.

CONCLUSIONS

1. Alterations in the acid-base balance of the blood of new-born infants may be produced by the daily ingestion of small amounts of alkali-producing salts.

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19. Faber, H. K.: Hydrochloric Acid Milk in Infant Feeding, Am. J. Dis. Child. **26**:401 (Nov.) 1923.

20. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, New York, D. Appleton and Company, 1923, pp. 118 and 123.

21. Griswold, C., and Shohl, A. T.: Gastric Digestion in New-Born Infants, Am. J. Dis. Child. **30**:541 (Oct.) 1925.

2. The acid-base balance of older infants is affected only by amounts of alkali greater in proportion to body weight than those effective in new-born infants. A greater lability of the acid-base balance of the blood of new-born than of older infants is indicated.

3. The diminution in the alkali reserve in new-born infants produced by the ingestion of cow's milk may be compensated by the daily addition of approximately 0.25 Gm. of sodium bicarbonate to the formula.

4. Greater increases in weight were observed in infants who received sodium bicarbonate and citrate in addition to cow's milk dilutions than in those who received similar formulas without added alkali.

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ENCEPHALITIS AS A COMPLICATION OF MEASLES

A REPORT OF THIRTEEN CASES

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During the past year, Milwaukee has experienced an extensive epidemic of measles. The total number of reported cases was 15,001 for the epidemic year (1931-1932), during which time we recognized most of our cases of encephalitis. During the months that the epidemic assumed its greatest proportions, the cases complicated with encephalitis increased proportionately in number. The patients for whom hospitalization was requested were admitted to the South View Hospital or to the Milwaukee Children's Hospital. In a collaboration of the records of the two institutions, we are able to present briefly the report of thirteen cases of encephalitis complicating measles, and the necropsy report on three of these. This series includes the largest number of cases observed during one year (one epidemic).

Neal and Applebaum [1] suggested that the recent increasing incidence may be due to greater interest in this condition. The great majority of cases have been reported in the past six years. The literature for the past century contains only a sprinkling of sporadic cases of measles complicated by nervous symptoms. Barlow and Penrose [2] reported the first studies on the pathologic process. Bergenfeldt,[3] Mosse and Creutzfeld,[4] and Brock [5] reported on the pathologic observations. Some authors have limited their report to the clinical picture, others to the

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1. Neal, Josephine B., and Applebaum, Emanuel: Encephalitis Associated with Measles, Bull. New York Acad. Med. **3**:414 (June) 1927.

2. Barlow and Penrose: On a Case of Early Disseminated Myelitis, Tr. Med.-Chir. Soc., London **70**:77, 1887.

3. Bergenfeldt, E.: Myelitis als Masernkomplikation, Acta med. Scandinav. **61**:281, 1924.

4. Mosse and Creutzfeld: Zwei Fälle von akuter Gehirndegeration nach Masern, Jahrb. f. Kinderh. **62**:272, 1926.

5. Brock, J.: Ueber Systematik und Klinik der Meningoencephalitischer Krankheitszustände im Kindesalter, Ztschr. f. Kinderh. **40**:552, 1925-1926.

pathologic aspect. Lowenburg [6] cited encephalitis in a case of hemorrhagic measles. Todesco [7] reported a case in which the patients showed unusual nervous symptoms. Neal and Applebaum reported twelve cases; the onset was usually sudden and developed during, or a few days after, the attack of measles. Fever and headache were almost constant symptoms; convulsions were present in about half of the cases. The most striking of all the symptoms were changes in the mental condition, varying from mild degrees of irritability or apathy to profound stupor or delirium. The physical signs were chiefly those due to varying degrees of meningeal irritation or increased intracranial pressure.[1] Further investigation reveals case reports by de Mare,[8] Bruce,[9] Atwell,[10] Miller [11] and Heath.[12]

Musser and Hauser [13] reported ten cases of encephalitis with a summary of two cases and the protocol of the necropsy record. There was marked injection of the vessels and capillaries of the brain and a general and diffuse parenchymal round cell infiltration, and particularly around the blood vessels many small hemorrhages were seen. Perivascular hemorrhages were also reported about some of the small vessels of the brain. These authors found no evidences of injury to the vascular endothelium. Ferraro and Scheffer [14] reported on the pathologic changes and interpretation in six cases of encephalitis and encephalomyelitis complicating measles. The six cases reported showed lesions that were practically the same in all. They consisted mainly of a perivascular proliferation formed especially by microglial elements. In some of the cases there were hematogenous elements (mainly lymphocytes) in the perivascular areas. Accompanying the perivascular proliferation there was a concomitant perivascular demyelinization, which forms another characteristic of the pathologic process. There was also a thickening of the endothelium of the blood vessels.

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6. Lowenburg, H.: Hemorrhagic Measles with Encephalitis, Arch. Pediat. **43**:73 (Feb.) 1926.

7. Todesco, J.: A Case of Measles Showing Unusual Nervous Symptoms, Lancet **2**:21 (July 3) 1926.

8. de Mare, Felice: A Case of Encephalitis After Measles, Pediatria **35**: 1183 (Nov.) 1927.

9. Bruce, James: Encephalitis Following Measles, Kentucky M. J. **27**:278 (June) 1929.

10. Atwell, J. C.: Encephalitis as Sequela of Measles, Pennsylvania M. J. **34**:253 (Jan.) 1931.

11. Miller, Milo: Measles Encephalitis, J. A. M. A. **97**:161 (July 18) 1931.

12. Heath, Parker: Measles Encephalitis, Am. J. Ophth. **15**:130 (Feb.) 1932.

13. Musser, J. H., and Hauser, G. H.: Encephalitis as a Complication of Measles, J. A. M. A. **90**:1267 (April 21) 1928.

14. Ferraro, Armando and Scheffer, F. H.: Encephalitis and Encephalomyelitis in Measles: A Pathologic Report of Six Cases, Arch. Neurol. & Psychiat. **25**:748 (April) 1931.

OUR SERIES

We have studied thirteen cases of encephalitis complicating measles. One of our patients was seen in 1927, two in 1929, one in 1931 and

TABLE 1.—*Data in Authors' Cases*

No.	Patient	Sex	Age	Onset, Days After Rash	Admitted, Days After Onset of Encephalitis	Admission Temperature, Rectal	Symptoms	Signs
1	G. R.	M	6 yrs.	4	1	102.4	Drowsiness; anorexia; headache	Brudzinski; Kernig; scaphoid abdomen; later twitching upper extremity and face
2	L. R.	M	13 mos.	4	2	103.8	Stupor; dyspnea	Brudzinski; Kernig
3	G. S.	M	4½ yrs.	2	2	.....	Stupor; emesis	Dilated, fixed pupils; scaphoid abdomen
4	C. C.	F	4½ yrs.	5	9	102.4	Aphasia; drowsiness; shallow respirations	Absent deep reflexes; Babinski; scaphoid abdomen
5	R. T.	M	8 yrs.	4	15	99.4	Convulsions; restless, irritable unable to raise self or speak	Rigidity of both upper extremities; patellar reflexes increased
6	C. K.	M	5 yrs.	8	3	101.2	Drowsiness; anorexia; restlessness	Head retraction; Babinski; fine tremor of upper extremities; abdomen scaphoid; rigidity extremities
7	L. T.	F	7½ yrs.	3	2	103.8	Drowsiness; pain in lower extremities	Rigidity of neck
8	F. G.	F	5 yrs.	4	1	99.4	Stupor; irritability; convulsions	"Lead pipe" rigidity; stiff neck; Babinski; patellar reflexes absent
9	E. L.	M	8 yrs.	6	1	99.4	Stupor; emesis; restless; dizziness; convulsions on left side	Neck rigid
10	W. L.	M	5½ yrs.	4	2	97.6	Drowsiness; anorexia; emesis; restless	Patellar reflexes increased
11	J. V.	M	5 yrs.	3	2	103.0	Drowsiness; convulsions	Brudzinski; coma
12	J. D.	F	2 yrs.	5	..	.....	Drowsiness	Rigid neck; spasticity of lower extremities
13	E. D.	M	10 mos.	6	..	.....	Drowsiness	Flaccid lower extremities

nine within a period of three months in 1932. The mortality was 43 per cent; three patients died in 1932, one in 1931 and two in 1929. The ages ranged from 13 months to 8 years, inclusive. There were nine boys and four girls; only one girl died.

The cases conform to the typical picture as reported, in that in twelve the onset occurred between two and six days after the onset of the rash, and in one eight days after. In all but one the encephalitis

began with stupor or drowsiness, and in this case the onset was characterized by restlessness and convulsions. Two patients were drowsy and had convulsions. Thus three had convulsions at the onset. Six patients had a rectal temperature above 99.4° F. on admission. The physical findings revealed rigidity of the neck in five cases, a positive Brudzinski neck sign in three and a diversity of other neurologic signs which often varied from day to day.

TABLE 2.—*Laboratory Findings*

	Blood		Spinal Fluid						
No.	Leukocytes	Neutrophils, per Cent	Days After Onset	Pressure	Cells	Globulin	Sugar	Colloidal Gold Reaction	Outcome
1	20,000	78.0	5	Increased	85 lymphocytes 69%	++	125	—	Recovered; mental impairment
2	17,000	82.5	2	Increased	112	0	92	Negative	Died of pneumonia
3	.....	....	2	Increased	112	0	120	—	Died; necropsy
4	23,600	83.0	5	Increased	20 lymphocytes 50%	—	116	Negative	Died; necropsy
5	16,200	84.0	15	Normal	7	+	...	.....	Recovered completely
6	12,600	80.0	11	Normal	5	+	74	1342100000	Died; necropsy
7	14,200	74.0	3	Normal	50	Trace	...	.....	Recovered
8	16,000	78.0	0	Normal	7	0	71	2344432000	Recovered
9	15,600	76.0	..	Normal	21	0	84	.....	Died
10	18,000	83.0	2	Increased	79 lymphocytes 40%	++	...	1233320000	Recovered completely
11	26,000	83.5	2	Increased	29 lymphocytes 40%	+	91	Negative	Recovered completely in 48 hours
12	15,200	82.0	..	Normal	20 lymphocytes 98%	..	...	.....	Recovered; seen in home by Dr. Fox
13	.....	....	..	Slight increase	380 lymphocytes 82%	..	...	.....	Died; seen in home by Dr. Fox

LABORATORY FINDINGS

Eleven of our patients (two were not so examined) exhibited a polymorphonuclear leukocytosis ranging from 12,600 to 26,000 leukocytes per cubic millimeter even up to fifteen days after the onset. The percentage of polymorphonuclears ranged from 74 to 84. Jenkins stated that "the blood may show a leukocytosis with high polynucleosis," [15] and others list a polymorphonuclear leukocytosis in their case reports. However, no one has emphasized the consistent feature of this condition.

15. Jenkins, P. K.: Measles and the Central Nervous System, J. Missouri M. A. **27**:65 (Feb.) 1930.

The spinal fluid findings were rather uniform. All fluids were clear, and seven were under increased pressure. The cell count ranged from 5 to 380, of which from 40 to 98 per cent were lymphocytes. The globulin was positive in six of the eleven fluids so tested. The sugar ranged from 71 to 125 mg. per hundred cubic centimeters in the eight fluids so tested. A colloidal gold test (Lange) was made on six fluids; in three it was negative. Three fluids showed the changes noted in table 2.

The spinal fluid findings apparently bear no relationship to the stage or the severity of the disease. The Wassermann and microprecipitation tests were negative in all.

PATHOLOGIC OBSERVATIONS

Necropsy was performed on three patients (nos. 3, 4 and 6). The findings of interest were limited to the brain. They were essentially the same in all three cases. Grossly, there was a marked congestion of the pial vessels. The microscopic changes, as reported by Dr. Fernan-Nuñez who studied the sections, showed a fibrotic thickening of the vessel walls, hyperplasia of the endothelium and in places small red thrombi and petechial hemorrhages. There was generally an increase in neuroglia around the affected nerves and vessels, together with an increase in the microglia. There were fatty changes in the myelin, the axis cylinders usually being unaffected, and the tissues in the neighborhood presented a somewhat moth-eaten appearance. There were discrete areas which appeared acellular due to the disappearance of pyramidal cells. In some of the large pyramidal cells the Nissl bodies had disappeared and the cells were shrunken. As a general rule, the pathologic changes appeared to predominate in the white substance, extending in places even to the gray areas.

TREATMENT

Treatment varied greatly according to the presenting symptoms and the condition of the patient. No one system of treatment was followed in a large enough group of cases to warrant conclusions. Convalescent serum given intramuscularly, transfusion of whole blood, intravenous injections of dextrose solutions and stramonium all produced symptomatic results. The most striking result in this series was obtained in the treatment of J. V. This patient was brought to the hospital in a convulsion. After spinal drainage, he was given 5 cc. of a 20 per cent solution of magnesium sulphate intravenously (slowly), but the convulsion continued. Half an hour later he was given 10 cc. of a 50 per cent solution of magnesium sulphate intramuscularly. The con-

vulsion continued, and half an hour later he was given 1 grain (0.065 Gm.) of sodium amytal hypodermically. This injection had no effect in half an hour, and chloroform was given by inhalation until the convulsion stopped. Following this, the patient was given 2 ounces (59.2 cc.) of 50 per cent magnesium sulphate solution by mouth or rectum every two hours for two days. In forty-eight hours the child appeared perfectly well and made an uneventful recovery.

SUMMARY

Three theories have been proposed in the explanation of encephalitis complicating measles: (1) the result of a virus independent of measles, (2) an allergic or anaphylactic phenomenon and (3) a virus activated by the measles organism. On the basis of the remarkable consistency in the clinical picture and findings in most established cases of encephalitis complicating measles, viz., time of onset in relation to the rash, the fever, the drowsiness or convulsions, the polymorphonuclear leukocytosis, the pleocytosis and increased sugar in the spinal fluid and the pathologic changes, we are inclined to believe that the condition is a clinical entity produced by some specific virus or organism.

CONCLUSIONS

The encephalitis complicating measles appears to be a definite clinical entity. The complication occurs in young children, usually between 2 and 8 years of age. The onset is rather sudden, within twenty-four hours, on about the fourth day after the rash of measles appears. The symptoms are usually drowsiness or stupor, or convulsions. There may be irritability, restlessness, anorexia or emesis as well. On examination, the child is usually comatose, has a slight fever and presents a variety of neurologic signs which may vary from day to day.

ACUTE PYOTHORAX

TREATMENT OF CHILDREN AND INFANTS BY ASPIRATION OF PUS AND AIR REPLACEMENT: A PRELIMINARY REPORT

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It is the purpose of this report primarily to draw attention to the method of therapy. This procedure was first introduced by Parker;[1] since then Potain,[2] Forlanini,[3] Morelli,[4] Elias,[5] Danna[6] and others have published their observations. To our knowledge this is the first report on its use in children and infants exclusively.

PROCEDURE

Simply stated, the principle of this treatment is the aspiration of pus and the replacement by air. The apparatus consists of a 30 cc. Luer syringe and a large needle.

Fairly certain location of the empyema should be made clinically and roentgenologically. The patient is placed in either a horizontal or a sitting position. The proper intercostal space is chosen. The left thumb is pressed against the lower border of the upper rib, thus protecting the intercostal artery, vein and nerve. The needle is inserted through the intercostal space directly beneath the thumb, and the syringe is attached. In this manner, the vessels are rarely injured. By the aspiration of pus, it is definitely ascertained that the needle is in the empyema cavity. A syringe full of pus is then removed, and an equal amount of air is injected with the same syringe. This is repeated until on aspiration no pus enters the barrel. The injection of an additional 10 or 15 cc. of air will facilitate the aspiration of any remaining pus. Tappings are repeated every four to seven days.

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1. Parker, R. W.: Suggestions for the Treatment of Special Cases of Empyema by Thoracentesis and the Simultaneous Injection of Purified Air, Lancet **1**:689 (April 29) 1882.

2. Potain: Intrapleural Injections of Sterilized Air in the Treatment of Pleural Effusions Following Pneumothorax, Bull. Acad. de méd., Paris **19**:537, 1888.

3. Forlanini, C.: Treatment of Pleural Empyema, Policlinico **1**:269, 333, 353 and 385, 1890.

4. Morelli, E.: Wounds of Lung and Pleura, Boston, W. M. Leonard, 1920.

5. Elias, H.: Treatment of Acute Emypema of the Thorax with Artificial Pneumothorax, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **38**:543, 1924.

6. Danna, J. A.: The Treatment of Empyema by Aspiration and Air Replacement without Drainage, J. A. M. A. **96**:1453 (May 2) 1931.

WHAT PURPOSE DOES AIR REPLACEMENT SERVE?

Complete removal of pus by aspiration is mechanically possible with air replacement, and we have frequently seen the roentgen evidence of complete evacuation of an empyema cavity by this procedure. Davies [7] has demonstrated that simple aspiration cannot remove more than 50 per cent of the fluid.

Air is slowly absorbed. A negative pressure is gradually restored in the intrapleural cavity, exerting a steady traction force on the lung and permitting gradual reexpansion of the lung with eventual pleural contact.

Air creates a positive pressure. This produces immobilization and compression of the lung, with elimination of pulmonary tension, and, therefore, rest and healing.

Air prevents rapid changes in intrapleural pressure with their sequelae, edema of the lung, pain, cough and cardiac changes.

Air keeps the visceral and the parietal pleura separated until the inflammation subsides; thus adhesions do not occur or are slight in extent.

The natural mechanism of defense in exudative pleurisy is the separation of pleura and the compression of lung (Morelli [4]). Air replacement maintains this mechanism.

Finally, this procedure may shorten the term of illness by preventing the exit of infective material from the compressed lung.

OBSERVATIONS

It was noticed that pus, thick at the first tap, thins and flows easily by the second or third. Danna,[6] in some cases in which he encountered thick, fibrinous pus made a small intercostal incision. This was kept open with a clamp, while the pus was expelled in expiration or else withdrawn by the clamp. In a few cases the last tap revealed a thick, mucoid, brownish material.

High fever usually subsides following the first tap, and after two or three punctures, except in isolated cases in which the temperature reaches 100 F., the patient is free from fever.

After the first tap the patient experiences a noticeable feeling of well-being; he becomes interested in his surroundings, his appetite improves and his face becomes brighter. These observations are more striking with each successive tap, and soon the patient begins to take on weight.

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7. Davies, M. H.: Complete Removal of Pleural Effusions, Lancet **2**:1,774 (Dec. 28) 1912.

COMMENT

Fourteen patients with acute pyothorax following pneumonia were treated exclusively by this method. A study of fifty preceding cases was made for comparison. Of these, twenty-nine came to operation. The mortality was 21 per cent. Six patients required two operations; one required three. In two patients osteomyelitis of the ribs developed. Eliminating one patient in whom drainage continued for over two years and those that left the hospital before complete cure was obtained, only twenty cases could be reviewed for the length of time the cavities drained and the period of fever. In seventeen of them there were fever and drainage for more than fifty days.

The accompanying table shows the important data concerning our patients. The youngest was 6 months old. The number of days of

Table Showing Observations in Fourteen Cases

Number	Sex*	Color	Age	Side	Weight Gain, Pounds	Tappings	Fever, Days	Drainage, Days
1	♀	W	1½ yrs.	R	0	2	9	4
2	♀	W	5 yrs.	R	3	6	45	44
3	♂	W	7 yrs.	L	5½	7	41	35
4	♀	W	2½ yrs.	L	4	9	103	101
5	♀	B	5 yrs.	L	0	3	24	12
6	♂	W	10 mos.	Died				
7	♀	W	21 mos.	L	4	6	47	46
8	♂	B	9 yrs.	L	1	2	8	7
9	♀	W	2 yrs.	L	0	7	67	71
10	♀	W	7 yrs.	R	7	2	16	7
11	♂	W	2 yrs.	L	½	4	24	25
12	♂	W	2 yrs.	L	3	4	46	45
13	♂	W	3 yrs.	R	7	4	22	21
14	♂	W	6 mos.	L	0	6	30	26

* In the table, ♀ indicates female; ♂, male.

fever was counted from the first tapping. The period of drainage was considered as from the first to the last tapping. The only death occurred in the case of a 10 month old infant in which the condition was complicated by a bilateral otitis media and severe gastro-intestinal failure. It will be noted that in only two patients did the period of fever and drainage extend beyond fifty days.

COMPLICATIONS

Pneumothorax with a pressure above atmospheric causes a slight emphysema at the site of puncture. This tension may be due to the pneumothorax itself or to the forced expiration of a crying or coughing child.

Signs of pleural irritation did not occur in any of our cases. One child whose confidence was difficult to obtain, showed pseudosigns of pleural irritation following one tap only. In another, during convalescence, a temperature of 104 F., rapid pulse and dyspnea suddenly developed, and the patient complained of violent abdominal pain.

The abdominal muscles were held rigid, suggesting an intra-abdominal lesion, but a pleural friction rub was present. In less than forty-eight hours the symptoms subsided. The condition was interpreted as the institution of pleural reflexes when the visceral pleura of the expanding lung came in contact with the parietal pleura. A pneumothorax would have relieved the symptoms immediately.

Cellulitis occurred in two cases. This complication may follow when the pneumothorax is under greater than atmospheric pressure, causing the blowing of pus into the soft tissues around the site of puncture while the needle is withdrawn. It may be avoided by withdrawing some air at the end of aspiration, when it is noticed that the intrapleural pressure forces the piston outward. Cellulitis may also occur if, when air is being injected, the needle point is displaced into the soft tissues, and pus is injected into the surrounding area. We believe that with reasonable care by the operator these accidents can be prevented.

CONCLUSIONS

Evaluation of this method cannot depend entirely on the statistics for the small number of cases here presented. Accepting the standards for the evaluation of a procedure for the treatment of empyema, it is evident that this method offers the least risk to the patient; there is no sacrifice of structure, with the danger of its ensuing deformities; it is simple and safe, and it does away with the pleura-irritating drains, which stimulate pus formation, and the crippling adhesions which so frequently lead to contractions of the thorax, loss of function and severe pressure and traction symptoms. Finally, since this method allows for complete evacuation of pus with complete reexpansion of the lung, it probably reduces the chances of recurrence and chronicity to almost a minimum.

SUMMARY

Fourteen infants and children with acute pyothorax, following pneumonia were treated by aspiration and air replacement. The procedure is outlined and the advantages are related, with the suggestion that this method should be submitted to greater clinical trial.

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GUANIDINE INTOXICATION

A COMPLICATING FACTOR IN CERTAIN CLINICAL CONDITIONS IN CHILDREN

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Increased concentration of guanidine bases in the blood has been reported in a variety of clinical conditions. Some of the studies along this line are those of Paton [1] and his associates in connection with parathyroid tetany, of Major and Weber [2] who attempted to associate guanidine with hypertension, of Minot and Cutler [3] and Ellsworth [4] in regard to the intoxication associated with liver injury, of Minot and Cutler [5] who found the guanidine increased in a few cases of eclampsia, and recently that of Dodd, Minot and Casparis [6] who regard guanidine as a complicating toxic factor in infantile diarrhea. Various methods have been used for the estimation of guanidine and no method yet available for this rather difficult determination is entirely satisfactory. Granting for the moment that the guanidine was really increased in all these instances, the variety of conditions is rather bewildering. Even more upsetting is the fact that in no particular clinical entity has the guanidine been found invariably increased. Thus, though

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1. Paton, D. N., and Findlay, L.: The Parathyroids: Tetania Parathyreopriva; Its Nature, Cause, and Relation to Idiopathic Tetany: IV. The Etiology of the Condition and Its Relation to Guanidin and Methyl Guanidin Intoxication, Quart. J. Exper. Physiol. **10**:318, 1916.

2. (*a*) Major, R. H., and Weber, C. J.: The Probable Presence of Increased Amounts of Guanidine in the Blood of Patients with Arterial Hypertension, Bull. Johns Hopkins Hosp. **40**:87, 1927; (*b*) The Possible Increase of Guanidine in the Blood of Certain Persons with Hypertension, Arch. Int. Med. **40**:891 (Dec.) 1927.

3. Minot, A. S., and Cutler, J. T.: Guanidine Retention and Calcium Reserve as Antagonistic Factors in Carbon Tetrachloride and Chloroform Poisoning, J. Clin. Investigation **6**:369, 1928.

4. Ellsworth, R.: Guanidine Base Concentration in Blood of Normal Individuals and in Patients with Liver Injury, Bull. Johns Hopkins Hosp. **46**:296, 1930.

5. Minot, A. S., and Cutler, J. T.: Increase in Guanidine-Like Substances in Acute Liver Injury and Eclampsia, Proc. Soc. Biol. & Med. **26**:607, 1929.

6. Dodd, K.; Minot, A. S., and Casparis, H.: Guanidine as a Factor in Alimentary Intoxication in Infants, Am. J. Dis. Child. **43**:1 (Jan.) 1932.

Paton's group [7] has demonstrated an increase following parathyroidectomy and their results have been confirmed by Kühnau [8] and Koch,[9] other observers [10] have found no increase in this condition. Minot and Cutler [11] found the guanidine consistently increased in acute injury to the liver, but failed to find this when equally extensive interference with hepatic function was accomplished more slowly. Some patients with eclampsia show an increase in guanidine; others do not.[12] Our preliminary finding of increased guanidine in the blood in intestinal toxemia has been repeatedly confirmed in this laboratory. However, increased guanidine does not accompany all diarrhea, nor is it found high at all stages of a given case in which high levels may be reached.

In the instances in which guanidine has been found high, there have usually been certain accompanying symptoms which are similar to those produced in experimental guanidine poisoning. The majority of investigators agree as to the symptomatic picture, manner of death and gross pathologic changes caused by guanidine. In the clinical studies much confusion has arisen because each investigator has attempted to ascribe the cause of the increase to the particular clinical entity under investigation. In the work we are reporting we hope to add additional evidence that the guanidine may be increased in the blood in a variety of clinical conditions, to bring out the similarity of the intoxication accompanying such increase and that of experimental guanidine poisoning, and to emphasize especially two underlying factors which may cause hyperguanidinemia. The procedure we have used to demonstrate increases in guanidine-like substances is also described.

CHEMISTRY AND TOXICOLOGY OF GUANIDINE

Guanidine is a nitrogenous base with the formula $C{=}\begin{smallmatrix}NH^2\\NH\\NH^2\end{smallmatrix}$. This group occurs in creatine (methyl guanidine acetic acid) and arginine

7. Burns, D., and Sharpe, J. S.: The Parathyroids: Tetania Parathyreopriva. Its Nature, Cause, and Relation to Idiopathic Tetany: V. Guanidin and Methyl Guanidin in the Blood and Urine in Tetania Parathyreopriva and in the Urine in Idiopathic Tetany, Quart. J. Exper. Physiol. **10**:345, 1916.

8. Kühnau, J.: Ueber den Nachweis von Guanidin- Substanzen in Blut bei parathyreogener Tetanie, nebst Bemerkungen über gleichseitiges Auftreten von Guanidinen im Urin, Arch. f. exper. Path. u. Pharmakol. **115**:75, 1926.

9. Koch, W. F.: The Occurrence of Methyl Guanidine in the Urine of Parathyroidectomized Animals, J. Biol. Chem. **12**:313, 1912.

10. Greenwald, I.: Are Guanidines Present in the Urines of Parathyroidectomized Dogs? J. Biol. Chem. **59**:329, 1924. Major, R. H.; Orr, T. G., and Weber, C. J.: Observations on the Blood Guanidine in Tetania Parathyreopriva, Bull. Johns Hopkins Hosp. **40**:281, 1927.

11. Minot and Cutler (footnotes 3 and 5).

12. Stander, H. J.: Blood Guanidine Base Concentration in Eclampsia, Am. J. Obst. & Gynec. **23**:373, 1932. Minot and Cutler (footnote 5).

(α amino δ guanidine valerianic acid) which are both widely distributed and important biologic substances. The source of guanidine and any definite understanding of the biologic relationship between the simple base and the more complex substances containing the group are still unsolved problems. In contrast to the complex derivatives, the simple bases have a marked pharmacologic action. For the most comprehensive studies of guanidine poisoning as well as a review of the literature, the reader is referred to the papers of Paton's group [13] and the work of Frank, Stern and Nothmann.[14]

The subcutaneous administration of a lethal dose (from 200 to 250 mg. per kilogram) of guanidine hydrochloride to a dog causes a severe generalized toxemia. The most conspicuous symptoms are neurologic and gastro-intestinal. At first there is a hyperexcitability manifested by restlessness, confusion and fibrillary tremors. This is followed by general clonic convulsions which are increased in frequency by outside stimuli, such as handling or startling the animal. Sometimes the convulsions are tonic in nature, and general extensor spasms with opisthotonus occur. At times the picture is indistinguishable from that of tetany, and is characterized by the same increased excitability to electrical stimulation. Later the hyperexcitability is superseded by apathy followed by coma. Death usually occurs about twelve hours after the dose is given. Throughout the period of intoxication there is a gastro-intestinal disturbance of increasing severity. At first, salivation and nausea are noted, followed by persistent vomiting and diarrhea. These symptoms are all compatible with increased activity of the parasympathetic system and may well indicate, as suggested by Frank, Stern and Nothmann,[14] that the autonomic system is included in the general hyperirritability. As the gastro-intestinal irritation progresses, the vomitus contains fresh and changed blood and more and more blood appears in the stools. The respirations, which are at first rapid, are frequently interrupted by a hacking cough and occasionally by laryngeal spasm. Later there is dyspnea of the "air hunger" type which may continue with increasing severity until death. In some subjects the respirations become slow and shallow in the later stages of intoxication, and death appears to be due to respiratory failure. The pulse rate is accelerated in the early part of the intoxication and then markedly slowed.

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13. Paton, N.: The Significance of Guanidine in the Animal Body, Glasgow M. J. **104**:97, 1925. Paton and Findlay (footnote 1).

14. Frank, E.; Stern, R., and Nothmann, M.: Die Guanidin- und Dimethyl Guanidin- Toxikose des Säugetiers und ihre physio-pathologische Bedeutung, Ztschr. f. d. ges. exper. Med. **24**:341, 1920.

As the absorption of the subcutaneous dose progresses, the guanidine level in the blood increases from the normal concentration of from 0.3 to 0.4 mg. to levels of from 1 to 4 mg. per 100 cubic centimeters. Irregularities in the blood sugar, as described by Watanabe,[15] Clark,[16] and Frank, Nothmann and Wagner,[17] are consistently seen. Early in the intoxication the concentration of sugar in the blood is usually moderately increased. Later, there is a gradual decrease until extreme hypoglycemia may be reached before death. The height of the preliminary rise as well as the rapidity of the subsequent fall is considerably influenced by the state of carbohydrate nutrition at the time guanidine is administered. An animal fed a high carbohydrate diet may have a marked rise and later only a moderate decrease from the normal sugar level though exhibiting all the other signs of severe guanidine intoxication. It is probable that part of the cause for these fluctuations in the blood sugar is, as suggested by Clark [16] and by later work of Minot,[18] a change in autonomic activity. The recent work of Staub,[19] however, indicates that the carbohydrate metabolism may be influenced more fundamentally. Staub, in an extensive study of the hypoglycemia induced by guanidine and by the guanidine derivative synthalin, has shown that the loss in blood sugar can be approximately quantitatively accounted for by an increase in lactic acid which accumulates in the tissues and then appears in the blood and urine. This finding has been confirmed in less complete investigations by Minot.[18] Staub attributed the rise in lactic acid to a failure on the part of the poisoned organism to oxidize and resynthesize lactic acid to its precursors in a normal manner. He was able to show an actual decrease in the amount of oxygen utilized by tissues poisoned with guanidine. Whatever the cause may be, lactic acid is found to be markedly increased in the blood, especially in the later stages of guanidine poisoning. This accumulation is probably mainly responsible for the decrease in alkali reserve reported by Watanabe [20] and is consistent with the "air hunger"

15. Watanabe, C. K.: Studies in the Metabolic Changes Induced by Administration of Guanidine Bases: I. Influence of Injected Guanidine Hydrochloride upon Blood Sugar Content, J. Biol. Chem. **33**:253, 1918.

16. Clark, G. A.: Interrelation of Parathyroids, Suprarenals, and Pancreas, J. Physiol. **58**:294, 1924.

17. Frank, E.; Nothmann, M., and Wagner, A.: Ueber die Guanidininhypoglykämie, Arch. f. exper. Path. u. Pharmakol. **115**:55, 1926.

18. Minot, A. S.: The Mechanism of the Hypoglycemia Produced by Guanidine and Carbon Tetrachloride Poisoning and Its Relief by Calcium Medication, J. Pharm. & Exper. Therap. **43**:295, 1931.

19. Staub, H.: Studien über Synthalinwirkung, Ztschr. f. klin. Med. **107**:607, 1928.

20. Watanabe, C. K.: The Relation Between the Tetanoid Symptoms of Guanidine Administration and the Condition of Acidosis, J. Biol. Chem. **34**:65, 1918.

previously described. In acute poisoning there is but little change in the nonprotein nitrogen of the blood. If the intoxication is more prolonged, there may be a gradually increasing retention of nitrogen. In spite of the close resemblance of the nervous symptoms to those of tetany and the curative effect of calcium medication, to be discussed shortly, we have always found the blood calcium in experimental guanidine intoxication to be within normal limits.

Larger doses of guanidine cause a more rapidly fatal intoxication and somewhat different symptoms. The hyperexcitable stage is either very transient or absent. The experimental subject soon becomes apathetic and lies in a semicomatose condition. The respirations are sometimes labored and sometimes slow and shallow. The heart rate is usually extremely slow. The symptoms of gastro-intestinal irritation are marked, and a condition of extreme acidosis and hypoglcemia is more quickly reached than following more moderate doses. When sublethal doses of guanidine are administered repeatedly over a longer period of time, milder symptoms of the same general nature and similar but less marked changes in the blood chemistry are produced. However, more advanced pathologic changes develop.

Postmortem examination of a dog following a single lethal dose of guanidine shows grossly a markedly hyperemic gastro-intestinal tract with numerous bleeding points. There is congestion of other organs, including the brain. Following a more prolonged intoxication, the gastro-intestinal tract may be ulcerated as well as congested. There are small extravasations of blood in the other congested viscera. The brain is markedly congested, soft and edematous. Sometimes there are large subdural hemorrhages but more often petechial hemorrhages in the substance of the brain and cord. The spinal fluid contains increased globulin and cells and sometimes blood. Thus far we have not studied the micropathology, nor is there any extensive study reported in the literature. Nothmann [21] reported histologic changes indicating damage to the cerebral cortex and pia, while Fuchs [22] described changes in the brain similar to those seen in encephalitis in man.

The antagonism of calcium salts to the action of guanidine has long been known and has been repeatedly demonstrated. The protective and curative action of calcium can be shown for the manifestations of guanidine poisoning so far as they have been studied. Führer [23]

21. Nothmann, M.: Weitere Beiträge zum Bilde der Vergiftung mit Guanidinen, Ztschr. f. d. ges. exper. Med. **33**:316, 1923.

22. Fuchs, A.: Analyse der Guanidinvergiftung am Säugetier: Experimentelle Encephalitis, Arch. f. exper. Path. u. Pharmakol. **97**:79, 1927.

23. Führer, H.: Curare Studien: I. Die periphere Wirkung des Guanidins, Arch. f. exper. Path. u. Pharmakol. **58**:1, 1908.

first showed that the fibrillary tremors produced in an isolated nerve muscle preparation can be abolished. Kühnau and Nothmann [24] concluded that in the intact animal the nervous manifestations of guanidine poisoning may be prevented or made to disappear. Burns and Watson [25] and Major and Stephenson [26] demonstrated that the effect on the heart and circulation can be abolished. Clark [16] found that the hypoglycemia can be relieved or prevented. This has been confirmed by Minot,[18] who showed that calcium medication also tends to prevent the accumulation of lactic acid in rats poisoned with guanidine. The papers of Watanabe [27] and Klinger [28] which reported failure to get relief in severely poisoned animals are frequently quoted. Neither of these investigators gave calcium intravenously. In view of all the positive evidence, it seems that their negative results must have been due to inadequate medication. In our experience the persistent intravenous administration of calcium salts has prevented or relieved symptoms of intoxication produced in dogs by the administration of guanidine in either single or divided doses in amounts sufficient to cause typical symptoms and death in untreated controls. The toxicity of sublethal doses of guanidine is greatly influenced by the previous state of calcium nutrition of the animal.[3] There is apparently no chemical antagonism between calcium and guanidine and relief from symptoms following medication is not accompanied by any prompt decrease in the level of guanidine in the blood. The neutralizing effect of calcium and guanidine becomes apparent only when they are allowed to act on physiologic mechanisms. Much further experimental work will be necessary before any adequate explanation of this action can be reached.

THE ASSOCIATION OF GUANADINE WITH NECROSIS

Minot and Cutler [3] associated an increase of guanidine with the intoxication produced by carbon tetrachloride. The possibility that guanidine was a factor in the intoxication was suggested by (1) hyper-

24. Kühnau, J., and Nothmann, M.: Ueber die Guanidintoxikose und ihre Beziehungen zur Tetanie, Ztschr. f. d. ges. exper. Med. **44**:505, 1924.

25. Burns, D., and Watson, A. M.: The Effect of Thyro-Parathyroidectomy on the Heart and Circulation: 1. Action on Nervous Control of the Heart, J. Physiol. **52**:88, 1918; II. Action of Guanidin on Heart of Frog, ibid. **53**:386, 1920.

26. Major, R. H., and Stephenson, W.: Further Studies on the Elevation in Blood Pressure Produced by Guanidine Compounds, Bull. Johns Hopkins Hosp. **35**:186, 1924.

27. Watanabe, C. K.: The Effect of the Administration of Calcium upon Blood Sugar Content in Rabbits with Guanidine Hypoglycemia, J. Biol. Chem. **34**:73. 1918.

28. Klinger, R.: Beiträge zur pharmakologischen Wirkung des Guanidins, Arch. f. exper. Path. u. Pharmakol. **90**:129, 1921.

irritability of the nervous system resembling tetany, (2) hyperemia and hemorrhage of the gastro-intestinal tract and (3) extreme hypoglycemia accompanied by increased lactic acid concentration in blood and urine. Perhaps the strongest argument that a guanidine-like substance was involved was the protective action of calcium salts when no reduction in total or ionized calcium in the blood could be demonstrated. The principal lesion caused by carbon tetrachloride has been described by Gardner and co-workers [29] as an extensive central necrosis of the liver. The large oral doses used in these experiments destroyed a majority of the liver cells within forty-eight hours. Without influencing the degree of liver injury, calcium medication prevented or relieved the symptoms of intoxication. Guanidine determinations on the blood of the animals with extensive necrosis showed increases to three or four times the normal level. These concentrations are comparable to those seen in experimental guanidine poisoning. Similar increases were noted following rapid necrosis produced experimentally by chloroform, arsenic or phosphorus, or seen clinically in arsenical hepatitis or acute yellow atrophy. It seemed for a time that failure of hepatic function might be the cause of an increase in guanidine. This explanation became less satisfactory when further studies of blood from dogs with typical cirrhosis and ascites following chronic carbon tetrachloride poisoning of one year's duration or longer, failed to show increased guanidine. Similarly, in patients with hepatic disease such as cirrhosis or obstructive jaundice, little or no increase was found. It becomes more and more apparent that in order to cause an accumulation of guanidine there must be acute, extensive necrosis.

It has been shown that during the autolysis of necrotic tissues lecithin is broken down, yielding cholin as one of the cleavage products.[30] The work of Sharpe,[31] Reisser [32] and others indicates that the guanidine group may be formed from cholin and urea. Wells [30b] mentioned methyl guanidine as one of the products of tissue autolysis. Experiments have not been carried through consecutively by one investigator with the idea of demonstrating the mechanism of

29. Gardner, G. H.; Grove, R. C.; Gustafson, R. K.; Maire, F. D.; Thompson, M. J.; Wells, H. S., and Lamson, P. D.: Studies of the Pathological Histology of Experimental Carbon Tetrachloride Poisoning, Bull. Johns Hopkins Hosp. **36**:107, 1925.

30. (*a*) Coriat, I. H.: The Production of Cholin from Lecithin and Brain Tissue, Am. J. Physiol. **12**:353, 1904. (*b*) Wells, H. G.: Chemical Pathology, ed. 5, Philadelphia, W. B. Saunders Company, 1925.

31. Sharpe, J. S.: Choline as a Precursor of Guanidine: The Decrease in the Amount of Choline in the Hen's Egg During Incubation, Biochem. J. **18**:151, 1924.

32. Reisser, O.: Weitere Beiträge zur Frage der Kreatinbildung aus Cholin und Betäin, Ztschr. f. physiol. Chem. **90**:221, 1914.

guanidine poisoning. Taken together, these observations suggest, however, a connection between rapid tissue destruction and an increase in this toxic base. Direct proof of the association by means of experiments in vitro though theoretically ideal is technically difficult. In order to produce autolysis in vitro as it occurs in the body, many factors, such as acid base equilibrium and bacterial action, must be controlled. Even then one is always confronted with the possibility that a certain product isolated may have been formed in the process of its separation rather than produced by autolysis. We have not attempted such a direct proof but present further evidence that guanidine finds its way into the blood stream from foci of necrosis. There seems to be no reason why the tissue undergoing autolysis need be liver.

The plant toxin, ricin, was selected as an agent to produce necrosis not localized specifically in the liver. The lethal dose of the pure toxin is extremely small.[33] Most commercial preparations contain impurities and so vary widely in toxicity. Doses of from 0.05 to 0.3 mg. per kilogram of the particular preparation which we used caused necrosis in various tissues as well as a necrotic area of several square centimeters at the site of subcutaneous injection. The animals either died within from five to ten days or were killed at the end of this time. Studies of the guanidine concentration in the blood showed no change for the first two or three days, but as necrosis progressed there was a gradual increase to levels of one or more milligrams per hundred cubic centimeters. These animals showed many of the typical symptoms of guanidine intoxication, though the picture was confused by the effects of ricin itself. A few typical figures illustrative of the results obtained in ten dogs are presented in table 1. These data give no evidence regarding the mechanisms involved but strengthen the hypothesis that guanidine increases in the blood stream as a result of tissue breakdown whenever it occurs.

ASSOCIATION OF INCREASED GUANIDINE WITH RAPID FLUID SHIFTS

The magnitude of the increase of guanidine in the blood should be influenced by the amount and rate of autolysis and also by the rapidity with which the cleavage products enter the blood stream. If guanidine is a product of tissue breakdown, the fluid which bathes the tissues probably contains a higher concentration than the circulating blood. When dehydration is rapid, as in severe diarrhea, interstitial fluid is drawn into the blood stream to replace the fluid lost.

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33. Ford, W. W.: Plant Poisons and Their Antibodies, Centralbl. f. Bakt. **58:** 129, 1913.

Experimental demonstration that such a fluid shift, even in the absence of greatly increased autolysis, gives a transient increase in the concentration of guanidine in the blood was obtained by producing dehydration in dogs. Acute withdrawal of fluid from the tissues was accomplished by the repeated intravenous injection of hypertonic saline solutions. Moderate but definite increases in guanidine resulted. Most of these experiments were done under barbital anesthesia. The animals passed large amounts of urine and defecated frequently. The stools were usually liquid and sometimes contained blood. If the subjects

TABLE 1.—*Results in Dogs Following Administration of Ricin*

		Mg. per 100 Cc. Blood			
Dog No.	Date	Nonprotein Nitrogen	Sugar	Guanidine	Comment
31-1-2	1/ 2/31	27	94	0.40	Preliminary sample; 0.25 mg. ricin per kilogram injected subcutaneously
	1/ 4/31	30	79	0.43	Thickening of tissue round site of injection
	1/ 6/31	33	117	0.69	Side becoming necrotic around site of injection
	1/ 7/31	39	115	0.73	Dog very sluggish; aroused with difficulty
	1/ 8/31	52	114	1.09	Unconscious; killed following taking of sample; large necrotic area at site of injection
31-1-3	1/ 2/31	34	80	0.43	Preliminary sample; 0.10 mg. ricin per kilogram injected subcutaneously
	1/ 5/31	37	104	0.37	Seems all right; rather quiet
	1/ 7/31	32	106	0.92	Weak, occasional twitching of paws as in tetany; moderate diarrhea; stools somewhat bloody
	1/ 9/31	30	74	0.96	Condition very poor; killed with chloroform; large necrotic area at site of injection
31-1-4	1/ 9/31	33	92	0.40	Preliminary sample; 0.10 mg. ricin per kilogram; dose divided—injected in two sites subcutaneously
	1/12/31	48	90	0.70	Very quiet; sides thickened and tender
	1/14/31	70	108	1.07	Very quiet; sides thickened and tender
	1/15/31	73	60	1.20	Very quiet; tissue breaking down at injection sites; killed with chloroform
31-1-7	1/12/31	30	91	0.37	Preliminary sample; 0.10 mg. ricin per kilogram; dose divided—injected in two sites subcutaneously
	1/14/31	33	73	0.80	Very quiet; moderate diarrhea
	1/16/31	48	65	0.89	Very weak; diarrhea; killed with chloroform

were conscious there was marked restlessness, confusion and convulsions as the dehydration progressed. It is unlikely that the increase in guanidine played an important part in the symptoms seen, but the experiments indicate that acute withdrawal of tissue fluid into the blood stream increases the concentration of guanidine in the blood. A moderate rise in guanidine was also observed when the animals became dehydrated as a result of lack of water intake. If this type of dehydration was hastened by high temperature or by increasing loss of fluid by occasional intravenous injections of hypertonic solutions, the increase became more marked. These subjects showed no convulsive symptoms but often had a diarrhea of moderate severity which may have been due to gastro-intestinal irritation from the increased guanidine. Typical

results obtained in these various types of dehydration experiments are included in table 2.

CLINICAL STUDIES

In the preliminary study, Dodd, Minot and Casparis [6] reported increased concentrations of guanidine in the blood of infants with alimentary intoxication. In this study the blood was taken at different

TABLE 2.—*Results in Dehydration Experiments*

Dog No.	Method of Dehydration	Date and Time of Sample	Mg. per 100 Cc. Blood: Nonprotein Nitrogen	Mg. per 100 Cc. Blood: Sugar	Mg. per 100 Cc. Blood: Guanidine	Comment
32-9-1	40 cc. 10× Ringer's* intravenously at 1:30 p.m., 2:35 p.m. and 4:35 p.m.	9/20/32 1:30 p.m.	28	87	0.44	Preliminary sample
		3:35 p.m.	25	93	0.69	Passed urine twice; several watery stools; vomited occasionally
		5:35 p.m.	31	133	0.78	Fibrillary tremors; general convulsions; died at 5:40 p.m.
31-5-10	Dog anesthetized with sodium barbital; 50 cc. 20% NaCl by vein at 9:35 a.m., 10:55 a.m. and 12:30 p.m.	5/26/31 9:35 a.m.	31	...	0.46	Preliminary sample
		10:55 a.m.	30	...	0.63	Passed 50 cc. urine and had several watery stools
		12:30 p.m.	28	...	0.69	Died following last injection; moderate congestion of gastrointestinal tract
31-2-12	Water withheld; dog kept at ordinary indoor temperature, 65-75 F.; fed cooked meat	2/20/31	30	87	0.37	Preliminary sample
		2/22/31	35	83	0.50	No symptoms
		2/23/31	36	82	0.54	No symptoms; given water following sample
		2/24/31	31	87	0.36	Normal
31-2-11	Dog in hot room, 100-102 F.; water withheld; fed meat and evaporated milk	3/ 9/31 a.m.	30	87	0.40	Preliminary sample
		3/10/31 p.m.	39	95	0.77	Very quiet; moderate diarrhea; stools contain small amount of fresh blood; water given following sample
		3/11/31	29	87	0.43	Dog appears normal
31-5-1	Water withheld; dog kept at ordinary room temperature; meat diet; given 50 cc. 50% dextrose solution by vein twice a day	5/13/31	31	..	0.43	Preliminary sample
		5/14/31	37	..	0.47	
		5/15/31	55	..	0.80	Very quiet; refused to eat
		5/16/31	50	..	0.72	Dog killed following sample; moderate hyperemia of gastrointestinal mucosa

* 10× Ringer's is Ringer's solution of ten times the usual concentration.

stages of the illness with widely variable results. So-called intestinal intoxication is a symptom complex which may be brought about in a variety of ways, but in infants is most often associated with severe diarrhea. When improper feeding, dirty milk or a localized respiratory infection is the etiologic agent, the severity of the diarrhea, dehydration and acidosis, together with the previous nutrition of the child, determine the seriousness of the illness. When the infant has dysentery or a generalized infection resembling influenza with a high fever and a tendency to leukopenia, the severity of the primary infection and toxemia

are as important as the amount of diarrhea and dehydration. Since several factors may combine in a given case, and since the picture produced is practically the same no matter what the etiology, it is often difficult on first examination to determine the primary cause of the disease. Guanidine appears to be a complicating factor in the symptom complex called intestinal intoxication, however it is produced. Experience based on the study of about one hundred infants has shown us when to expect the highest concentrations of guanidine in the blood. These concentrations are from 0.7 to 1.5 mg. per hundred cubic centimeters. Infants with such increases present a typical clinical picture. They are either very restless or comatose, their skin is gray, their hands and feet cold and they often vomit brown material. When the diarrhea itself, rather than infection, is the chief cause of intoxication, the highest concentrations of guanidine are found following a rapid loss of fluid. When dysentery or influenza is the cause, the guanidine may reach high levels even without marked loss of fluid and base. The first type is more nearly comparable to the instances of acute dehydration produced in experimental animals. If the dehydration and acidosis are adequately overcome by the administration of fluids and buffer salts and transfusions of blood or serum and the urinary flow is reestablished, the guanidine in the blood soon returns to a more normal level and the child appears much better. If the infant has been well nourished, recovery from this point on is usually rapid. When a long period of poor nutrition has preceded the acute illness, nutritional edema, rickets and general debility complicate and prolong the convalescence. Reinfection or lack of extreme care in feeding and administration of fluid may cause another rapid loss of fluid and precipitate a recurrence of the original toxic picture. The second type of infant is more nearly comparable to experimental animals with extensive necrosis. Although the effect of a generalized infection on the organism as a whole is not entirely understood, high fever, bacterial toxins and the inability of the patient to take food must all contribute to a rapid breakdown of tissue which may lead to a persistent increase in guanidine. Improvement following administration of fluid to infants with this type of illness is much less striking. The fever continues, toxic symptoms persist and the guanidine concentration in the blood remains high or even increases.

If the guanidine remains high owing to persistent infection or because the dehydration and acidosis are only partially overcome, symptoms of chronic guanidine poisoning develop, unless they are combated by adequate calcium medication. The diarrhea continues, the appetite remains poor and vomiting recurs. There is evidence of damage to the blood vessel walls. Petechiae may appear in the skin, the vomitus often

again contains changed blood and occasionally the stools become tarry. Nervous symptoms from restlessness, definite tremor and tetany to generalized spasticity or clonic convulsions may occur. In the latter instance the picture is sometimes that of encephalitis or meningitis. The spinal fluid may contain increased globulin and white blood cells and occasionally red blood cells but no organisms. Casts, albumin and red blood cells are frequently present in the urine. There is moderate but gradually increasing nitrogen retention. Death may occur soon after the onset of the illness, or the child may live for a considerable time, becoming markedly emaciated. One gets the impression that for a considerable time before death the tissues are practically functionless. Postmortem examination shows no very specific pathologic changes, except those due to the primary or terminal infection. There is usually hyperemia of the gastro-intestinal tract and of the brain. There are small extravasations of blood in many of the tissues. Parenchymatous degeneration is often found in the kidneys and liver.

There are many points of similarity in the intoxication of severe infantile diarrhea and that sometimes seen in certain other clinical conditions. Powers [34] has suggested that so-called intestinal intoxication is but a symptom complex associated with conditions widely diverse in etiology. The majority of children with pneumonia have neither symptoms of guanidine intoxication nor an increase in guanidine in the blood. We have, however, found increased guanidine when patients with pneumonia showed extreme restlessness which was unrelieved by sedatives, tetany in the absence of lowered blood calcium or alkalosis, or gastro-intestinal irritation. These symptoms were relieved by calcium medication, although, the primary disease was unaffected. We made the same observations in a few cases of chronic meningococcus meningitis, meningococcemia and severe rheumatic fever. Although, again, dehydration and tissue destruction may well be underlying factors, we have no real explanation to offer for the occasional development of this intoxication. Through the cooperation of the surgical service, we have been able to study several children with the late intoxication associated with severe burns. Again increases in guanidine were found when marked restlessness, outspoken symptoms of tetany or vomiting of blood occurred. Here the large necrotic burned area is probably the source of guanidine.

In table 3 are presented typical examples of the changes in blood chemistry found in severe toxemias in children. The studies of blood chemistry are not as complete as one might wish, because in many instances the infants were too small to spare the required amount of

34. Powers, G. F.: A Comprehensive Plan of Treatment for the So-Called Intestinal Intoxication of Infants, Am. J. Dis. Child. **32**:232 (Aug.) 1926.

TABLE 3.—*Changes in the Blo*

No.	Name, Age, Weight	Previous Feeding	Duration of Acute Illness, Days	Primary Disease and Complications	Date	Gastro-Intestinal Symptoms	Degree of Dehydration	Outstanding Signs of Toxemia	Temperature, F.	Hemoglobin Gm. per 100 Cc.
1	R. H. 8 mos. 16 lbs. 6 oz.	Artificial; good; cod liver oil	14 much worse 4	No parenteral infection	7/12/31	Diarrhea and vomiting	Severe	Gray, cold, drowsy, irritable when aroused	105.5	10.4
					7/14/31	Slight diarrhea	None	None	100.0	....
2	S. L. K. 1½ mos. 5 lbs. 10 oz.	Artificial; good; cod liver oil	1	Bilateral otitis media; prematurity	7/29/31	Severe diarrhea and vomiting	Severe	Drowsy, gray, cold	100.0	11.3
3	N. S. 5 mos. 6 lbs. 14 oz.	Artificial; very poor; no cod liver oil	4	Otitis media; marasmus; nutritional edema; thrush	9/29/31	Severe diarrhea	Extreme	Extremely restless	96.6	13.3
					10/3/31	Diarrhea and vomiting	Severe	.....	101.0	22.0
					10/9/31	Severe diarrhea	Marked	Extremely restless	104.6	19.0
4	B. J. P. 6 mos. 7 lbs. 8 oz.	Artificial; poor; Eagle brand milk; no cod liver oil	3	Otitis media; marasmus; bronchopneumonia	8/10/31	Moderate diarrhea and vomiting	Moderate	Drowsy	101.5	11.2
					8/19/31	Severe diarrhea	Moderate	Drowsy	102.5	10.4
5	B. J. 4 mos. 8 lbs. 15 oz.	Artificial; fair; no cod liver oil	3	Shiga dysentery; otitis media; bronchopneumonia	9/19/31	Severe diarrhea; pus but no blood in stools; vomiting	Moderate	Drowsy and later convulsions	103.0	85% Sahli
6	J. M. T. 3 mos. 8 lbs. 15 oz.	Artificial; good; cod liver oil	3	Influenza; prematurity; encephalitis	7/14/32	Diarrhea and vomiting	Moderate	Delirious, convulsions; rigidity, carpopedal spasm, apnea	106.0	11.9
					7/18/32	None	None	Slightly spastic	102.0	....
7	M. H. 15 mos. 17 lbs. 12 oz.	Artificial; fair; little cod liver oil	5	Influenza; encephalitis	7/15/32	Diarrhea, bloody stools	Moderate	Listlessness followed by convulsions, rigidity, tetany	103.8	11.9
8	H. A. C. 4 mos. 10 lbs. 15 oz.	Breast; little cod liver oil	Whooping cough 25 pneumonia 6	Whooping cough: pneumonia	4/5/31	Diarrhea	Moderate	Laryngospasm; tetany; rigidity	101.8	13.6
9	D. M. A. 21 mos. 17 lbs. 13 oz.	Artificial; very poor; no cod liver oil	13	Pneumonia	3/8/31	Vomiting and diarrhea	Slight	Carpopedal spasm; tetany; rigidity; extreme restlessness	105.0	45% Sahli
10	N. E. 36 mos. 38 lbs. 4 oz.	Fair	1	Pneumonia	2/1/31	Vomiting	None	Extremely drowsy; vomited brown material	101.0	....
11	B. D. M. 9 mos. 13 lbs. 6 oz.	Artificial; good; cod liver oil	18	Pneumonia and treated cretinism	1/28/31	None	None	Extreme restlessness; rigidity	105.0	70% Sahli
12	S. M. V. 72 mos. weight ?	Good	5	Extensive burn; septicemia; pneumonia	3/9/31	None	Mild	None	103.5	75% Sahli
					3/15/31	Moderate diarrhea	Mild	Tetany	104.0	....
					3/25/31	Vomiting and severe diarrhea	Mild	Tetany; vomited brown material	104.5	70% Sahli

* Hartmann's solution is made up as follows: 10 cc. contains lactic acid 85 per cent as sodium lactate, 0.6 cc.; sodi

White Blood Cells, per C.Mm.	Blood Chemistry: CO_2 Content, per Cent by Volume	Blood Chemistry: Mg. per 100 Cc.				Result	Comment
		Non-protein Nitrogen	Guanidine	Serum Calcium	Inorganic Phosphorus		
	p_H						
23,400	7.25	10.0	65	0.92	....	...	Recovered	Given Hartmann's solution* subcutaneously; sodium bicarbonate by vein; calcium gluconate in vein and muscle
.....	7.49	49.8	..	0.37	....	...	.....	Discharged in good condition 7/19/31
10,000	7.20	23.3	..	0.90	....	...	Recovered	Given Hartmann's solution* subcutaneously; sodium bicarbonate by vein; calcium gluconate in vein and muscle; rapid recovery
12,100	7.34	38.6	..	....	10.7	5.7	Recovered	Given large amounts of parenteral fluids and two transfusions; gained weight rapidly and became edematous
.....	7.25	33.0	33	0.92	....	...	.....	Lost 1¼ pounds during 2 days preceding these observations; given sodium bicarbonate by vein; transfusion 10/5/31; calcium gluconate by vein and in muscle
.....	7.12	10.9	..	....	....	...	.....	Following a second rapid fluid loss, due to increased diarrhea, given parenteral fluids; sodium bicarbonate by vein; later transfusions; slow recovery
18,900	7.43	46.0	..	0.40	....	...	Died	Given parenteral fluids; transfusion; calcium gluconate intramuscularly
24,000	7.27	36.0	30	0.85	....	...	.....	Parenteral fluids; sodium bicarbonate intravenously; calcium gluconate in vein and muscle; infection, fever and diarrhea persisted; terminal pneumonia
6,200	7.26	31.0	35	1.06	....	...	Died	Given sodium bicarbonate by vein; parenteral fluids; transfusions; calcium gluconate by vein completely relieved convulsions; lumbar puncture showed normal fluid; terminal pneumonia
6,200	7.15	52.0	57	1.08	....	...	.....	Parenteral fluids; Hartmann's solution;* vigorous treatment with calcium gluconate by vein and muscle; lumbar puncture showed normal fluid; temperature remained at 105-106 F. for about 4 days
7,000	....	....	22	0.46	....	...	Recovered	Much better; treatment continued less vigorously for a few days; uneventful recovery
20,850	7.40	55.5	..	1.00	....	...	Died	Treated vigorously with 5% dextrose and calcium gluconate intravenously; 4 hours after admission temperature 105.6 F.; spinal fluid normal; next morning patient comatose; temperature 106.6 F.; died 20 hours after admission
36,000	....	....	27	0.69	11.5	7.7	Recovered	Treated with parenteral fluids; Hartmann's solution;* transfusions; calcium gluconate by vein and muscle; guanidine normal 4/10/31; slow, uneventful recovery
17,200	7.52	54.6	30	0.64	10.1	2.3	Recovered	Had been in hospital 5 days previous to these observations; fever continuous 104 to 105 F.; had received parenteral fluids and transfusions; after this treated with calcium gluconate by vein and muscle; nervous symptoms relieved; gradual recovery
20,000	....	....	29	0.89	....	...	Recovered	Treated with calcium gluconate by vein and muscle; rapid improvement; discharged 2/8/31
12,800	....	39.0	..	0.86	....	...	Recovered	Sedatives without effect; became quiet following calcium gluconate by vein; lumbar puncture showed normal fluid; calcium medication continued several days; crisis and uneventful recovery
7,950	....	....	..	0.40	....	...	.....	Fresh burn; no toxic symptoms
26,500	....	....	30	0.94	12.6	...	.....	Burns becoming necrotic; intermittent calcium medication by vein and muscle; relief of tetany following each dose by vein
24,000	....	....	28	0.55	10.8	5.4	Died	Finally died of septicemia and pneumonia

*...oride, 1.5 Gm.; potassium chloride, 0.1 Gm.; calcium chloride, 0.05 Gm.

blood and, early in the investigation, we did not appreciate just what determinations were desirable. We have not yet studied lactic acid changes and have not included figures for blood sugar because the administration of dextrose by mouth and by vein made them too variable to be of significance. Extremely low blood sugar was not seen even before dextrose was given.

The first two cases presented illustrate intestinal intoxication in a well nourished child who has received adequate amounts of vitamins. Such children improve rapidly following administration of fluid. When the p_H and carbon dioxide are extremely low, we believe that it is better to give sodium bicarbonate intravenously than to rely on more conservative measures which subject the organism to acidosis for longer periods. Calcium medication is probably seldom necessary here, but like the bicarbonate seems to hasten recovery. Cases 3 and 4 illustrate the same toxic condition in marantic infants with parenteral infection. This type of case is much more difficult to manage. The first infant (N. S.) became edematous as a result of too rapid administration of fluid. Later, following a rapid loss of fluid, toxic symptoms accompanied by severe acidosis and a high concentration of guanidine appeared. Prompt adjustment of acid-base equilibrium with sodium bicarbonate, together with persistent calcium medication and more conservative administration of fluid and transfusions of blood led to a slow recovery. The second child (B. J. P.), though treated in the same manner, succumbed to an intercurrent infection.

Because loss of fluid is usually less acute, guanidine increase is not common in infants with dysentery or the diarrhea associated with generalized infection. However, when the primary infection is overwhelming, marked increases in guanidine may be found even when the degree of dehydration is only moderate. Case 5 illustrates hyperguanidinemia associated with Shiga dysentery. We have seen similar increases in children with the supposedly less toxic Flexner and Hiss-Russell types. Infants 6 and 7 were brought to the hospital in very hot weather because of diarrhea and vomiting. These symptoms, however, were secondary to an influenza-like infection. Although the dehydration was only moderate, the guanidine concentrations were very high. There was no prompt improvement following administration of fluid. Symptoms of tetany and encephalitis developed in both infants. They were treated vigorously with fluids given parenterally and calcium gluconate, but owing to differences in the nutrition or to the severity of the infection, only the first (J. M. T.) recovered. In these instances the diagnosis of encephalitis was made on the basis of symptoms and in the absence of changes in the spinal fluid. Experimental encephalitis with spinal fluid changes can be induced by the repeated administration of small

toxic doses of guanidine for a considerable period. Larger single doses cause congestion and edema of the brain without spinal fluid changes.

The sporadic occurrence of hyperguanidinemia as a complicating factor rather than as an essential feature of a disease is well illustrated in pneumonia. Cases 8, 9, 10 and 11 are illustrative of pneumonia complicated by intoxication. The last case (S. M. V.) illustrates that the necrotic tissue resulting from an extensive burn may cause an increase in guanidine in the blood accompanied by the typical picture of intoxication. In this instance and in several other severely burned children the symptoms referable to guanidine were relieved by calcium therapy.

While there are doubtless other toxic agents present which we have not studied, the figures presented indicate that guanidine may increase in a variety of clinical conditions. The concentrations reached are of a magnitude which if persistently maintained in an otherwise normal animal will cause gastro-intestinal irritation, nervous disturbances, reduced tissue oxidation and a tendency to extravasations of blood. Certainly the presence of such a toxic agent cannot be ignored in clinical conditions in which these symptoms are prominent features. The usual methods of treatment which restore fluids and increase urinary output tend to eliminate guanidine. The use of calcium which is specifically antagonistic to the action of guanidine has, in our experience, proved to be a valuable supplement to these measures. This is especially true when extensive and persistent tissue destruction, either localized or diffuse, tends to maintain an increased concentration of guanidine. The best defense we yet know against such an increase is to maintain as constantly as possible in the blood and tissues an increased supply of calcium ions. In experimental animals this may be accomplished by the administration of calcium, parathormone or acid. Only the repeated intravenous injection of calcium salts is adequate when the intoxication is severe before medication is started. When treatment is started earlier, the less radical measures suffice.

In the treatment of infants and children, safe and adequate calcium medication is more difficult. In many instances the calcium nutrition has been poor for weeks before the onset of the acute illness. Such patients are far more susceptible to increased guanidine, as were the experimental animals deliberately kept on a low calcium diet. Diarrhea and vomiting frequently make oral medication ineffective and inadvisable even early in the intoxication when, if the doses could be retained and absorbed, they might be adequate. Administration of acid is undesirable in persons who already have a tendency toward acidosis. We have so far had little experience with the use of para-

thormone. In mild intoxication without severe gastro-intestinal symptoms we give calcium salts and vitamin D orally. For more severe intoxication in which rest of the gastro-intestinal tract seems imperative, we give calcium gluconate solution both intravenously and intramuscularly. Intramuscular injections have the advantage of providing a persistent source of calcium, but the absorption is too slow to control a severe intoxication. Ideal intravenous medication should furnish a definite but moderate increase in calcium constantly. Injections given three or four times a day approach this ideal and give good results, the main difficulty being repeated venipuncture in small children. The dangers of acute hypercalcemia must always be kept in mind and the dose regulated accordingly. We have found 5 cc. of a 10 per cent solution of calcium gluconate [35] for infants and doses up to 10 cc. for larger children safe if given slowly. Our practice is to dilute the contents of the original ampule with 5 per cent solution of dextrose. Recently, in severe intoxication in which prolonged medication is necessary, we have combined intravenous calcium medication with the constant drip method described by Karelitz [36] for the administration of fluids. This method introduces calcium more slowly and evenly and obviates the difficulty of frequent venipunctures. Whenever calcium gluconate solution is used parenterally, leakage into the subcutaneous tissues must be avoided or local irritation will result.

ESTIMATION OF GUANIDINE-LIKE SUBSTANCES IN BLOOD

The only available method which is practical for the detection of guanidine bases in the small amounts of blood which can safely be withdrawn from infants is a colorimetric procedure. The method has been developed through the work of Marston,[37] Pfiffner and Myers [38] and Major and Weber [39] from a color reaction originally described by Tiegs.[40] Many criticisms can justly be made of this method. The

35. The calcium gluconate used both clinically and experimentally was furnished by the Sandoz Chemical Company.

36. Karelitz, S., and Schick, B.: Treatment of Toxicosis with the Aid of a Continuous Intravenous Drip of Dextrose Solution, Am. J. Dis. Child. **42**:781 (Oct.) 1931.

37. Marston, H. R.: Colorimetric Method for the Estimation of Guanidine and Methyl Guanidine, Australian J. Exper. Biol. & M. Sc. **1**:99, 1924.

38. (*a*) Pfiffner, J. J., and Myers, V. C.: The Colorimetric Estimation of Methyl Guanidine and Biological Fluids, Proc. Soc. Exper. Biol. & Med. **23**:830, 1925-1926; (*b*) On the Colorimetric Estimation of Guanidine Bases in Blood, J. Biol. Chem. **87**:345, 1930.

39. Weber, C. J.: The Determination of Guanidine Bases in the Blood, Proc. Soc. Exper. Biol. & Med. **24**:812, 1927. Major and Weber (footnote 2).

40. Tiegs, O. W.: Color Test for Guanidine Bases Together with Some Physiological Applications, Australian J. Exper. Biol. & M. Sc. **1**:93, 1924.

test does not distinguish between guanidine and methyl guanidine and is not entirely specific for the guanidine group. Some substances which are always present in blood, notably creatine and urea, give a certain amount of color with the reagent used, while uric acid and salts, especially ammonium salts, depress the development of the color. Each investigator who has used this method extensively has realized these difficulties and has devised various means of removing, or of correcting for, interfering substances. Little claim can yet be made for the absolute accuracy of the figures obtained or the identity of the substance measured. In spite of these limitations, the test when properly controlled gives results which are extremely valuable as an index to the type of intoxication dealt with and the therapy indicated. A low concentration of what is apparently guanidine is consistently found in normal blood and in the blood of the majority of sick persons. Whenever marked increases are found, they are accompanied by symptoms and pathologic changes which resemble those seen in experimental guanidine intoxication and which can be relieved in a similar manner by calcium therapy. If the substance measured is not guanidine or methyl guanidine, it is some as yet unrecognized substance the physiologic action of which is very similar to guanidine. We have called this substance guanidine in our discussion of clinical findings.

TECHNIC

The procedure used for the determination of guanidine in the work presented is essentially the earlier method described by Major and Weber [28] with a few minor changes which have been added during five years' experience. The estimation is carried out on protein-free filtrates prepared from blood by the method of Folin and Wu.[41] This filtrate contains the interfering salts and nonprotein extractives of blood and the guanidine in far too great dilution for colorimetric estimation. Before the color test is made, most of the salts are removed, creatine is converted to creatinine and the guanidine concentrated in a small volume of solution. The exact procedure follows:

Ten cubic centimeters of oxalated blood (less if this amount is not available though it is not advisable to attempt the determination on less than 6 cc. of blood) is diluted with seven volumes of water, and one volume each of 10 per cent sodium tungstate and two-thirds normal hydrochloric acid are added and thoroughly mixed. After standing half an hour or more, the precipitated protein is removed by centrifugation in order to get the greatest possible yield of filtrate. The supernatant liquid which may contain some floating particles is filtered through a small filter. A nonprotein nitrogen determination is made on 5 cc. of this filtrate. Fifty cubic centimeters (or as much as is available) of the same filtrate is evaporated slowly to dryness, being allowed to boil gently on a hot plate. The amount of creatine usually present in 50 cc. of filtrate representing 5 cc. of blood is largely converted

41. Folin, O., and Wu, H.: A System of Blood Analysis, J. Biol. Chem. **38**: 81, 1919.

to creatinine by this procedure, though the process is hastened by making the solution slightly acid by the addition of 1 cc. of two-thirds normal hydrochloric acid before the evaporation. Great care must be taken that no charring of the residue occurs as the last drops of water evaporate. The guanidine is removed from the dry residue by repeated extractions with small amounts of absolute alcohol. Most of the salts are excluded by this procedure because of their insolubility in alcohol. The successive alcoholic extracts are filtered through small filter paper and the total of from 40 to 50 cc. of filtrate evaporated to dryness on a hot plate or steam bath. As the evaporation proceeds, small amounts of distilled water (from 1 to 2 cc.) are added as the solution tends to become turbid as the volume of alcohol decreases. This addition of water clears up the turbidity until a small volume remains, decreases the tendency to "bumping" and also makes it easier to filter out the slight turbidity of the subsequent solution before making color comparisons. Again it is important that no charring is allowed to occur as the last drops of liquid evaporate. It is also important that the last trace of alcohol be removed, as alcohol gives a color with the reagent used. The slight residue left after this evaporation should be perfectly dry and white. This residue is dissolved in 5 cc. of water and 1 cc. of the freshly prepared guanidine reagent to be described is added. The resulting solution is filtered through a small high grade filter paper. The filtrate should be clear, as any turbidity interferes seriously with the comparison of colors. If filtering will not yield a clear solution, the addition of a small amount of barium carbonate before filtering may be helpful. We have, however, found this unnecessary if water is added during the evaporation of the alcohol and a good grade of filter paper is used.

Standards for comparison are prepared with varying amounts of guanidine in 5 cc. of distilled water to which 1 cc. of the color reagent is added. These are conveniently made up from a dilute standard solution of guanidine hydrochloride containing 0.02 mg. of guanidine per cubic centimeter. One cubic centimeter of this solution diluted to 5 cc. with water gives the 0.02 mg. standard. Two cubic centimeters is diluted in the same manner for the 0.04 mg. standard. A stock standard solution from which the less concentrated working standard is diluted contains 1 mg. of guanidine per cubic centimeter. This solution is kept preserved with toluene in the icebox and remains unchanged at least for several months. A standard containing 0.02 mg. of guanidine is usually required for comparison with the color obtained when a determination is made on 50 cc. of filtrate representing 5 cc. of normal blood. Abnormal blood may require standards as high as 0.1 mg. When unknowns are being analyzed, it is well to prepare a series of standards, e. g., 0.02, 0.03, 0.04 and 0.05 mg., and to choose the standard color which is nearest the unknown for comparison, because, as in all colorimetric work, it is not advisable to read against a standard which is very different from the unknown solution.

We make our color comparisons in a colorimeter, but approximately as good results can be obtained by comparing the colors in small tubes of uniform size and quality of glass, as is done in p_H determinations. If this method is used it is well to prepare a series of standards varying by only 0.005 mg. to make possible closer estimation of the amount of guanidine in the unknown. Both standard and unknown solutions should stand about ten minutes before the colorimetric reading is made. Fresh standard colors have to be prepared each time color comparisons are to be made, as the colored solutions become turbid after standing a few hours. From the colorimetric reading and the amount of filtrate used, the amount of guanidine in 100 cc. of blood can readily be calculated.

The color reagent which we use is the same as that described by Minot and Cutler.[3] It is made as follows:

10% sodium nitro-prusside	1 part
10% potassium ferricyanide	1 part
10% sodium hydroxide	1 part
Distilled water	3 parts
3% hydrogen peroxide	1 part

The solutions are kept in a dark place, and a small amount of the reagent mixed for use each day. The prepared reagent should stand about thirty minutes before it is used and should be a pale greenish yellow. One cubic centimeter of the solution gives an appreciable orange color when added to 5 cc. of solution containing as little as 0.02 mg. of guanidine. With larger amounts of guanidine, the color becomes a reddish orange.

It will be noted from the foregoing description that we have not adopted the procedure suggested later by Major and Weber [2b] and further elaborated by Pfiffner and Myers [38b] which offers an apparently ideal means of avoiding the difficulties due to salts, urea and creatine. These investigators adsorb creatine and guanidine onto charcoal directly from the original Folin-Wu filtrate, after making it slightly alkaline. The urea is left together with the salts and other unadsorbed extractives in the solution, which is discarded. The creatine and guanidine are then removed together from the charcoal by an overnight extraction with acidulated alcohol. From this point on, one is offered the alternative of adopting the procedure of Major and Weber who determine creatine in an aliquot and correct for it in the colorimetric result obtained, or of converting the creatine to creatinine as suggested by Pfiffner and Myers. Theoretically, this method has everything to recommend it, but in our hands recoveries have been so variable that we have not adopted it as part of the procedure used in our clinical studies. The conversion of creatine to creatinine minimizes this source of color increase since creatinine has been shown by Weber [42] to give only $\frac{1}{310}$ as much color as an equivalent amount of guanidine. Recoveries of guanidine in the presence of added urea show that amounts of urea normally present in blood contribute only a slight amount to the color obtained. In studying changes in guanidine concentration in blood from nephritic patients in which the content of urea fluctuates widely, it becomes necessary to correct for the varying interference. If, however, as in the investigation reported here, the blood specimens to be studied show but little variation in nonprotein nitrogen concentration, the color contributed by urea is practically constant. This slight error can be ignored as long as the emphasis is on the comparative rather than the absolute values obtained. This has been done in the results which we report. By the procedure just described the concentration of "guanidine" in normal blood is about 0.35 mg. per hundred cubic centimeters. In severe toxemia we frequently find a threefold or fourfold increase which cannot be accounted for by an increase in any known interfering substance.

SUMMARY

1. A résumé of what is known regarding the chemistry and toxicology of guanidine has been given.

2. We have shown that increases in guanidine or some closely related substance occur in the blood of experimental animals following

42. Weber, C. J.: The Determination of the Guanidine Bases in Urine, J. Biol. Chem. **78**:465, 1928.

rapid and extensive tissue necrosis or a sudden withdrawal of interstitial fluid into the blood stream.

3. Similar increases were found in the intoxications associated with a variety of clinical conditions.

4. In our experience the highest concentrations of guanidine occurred in patients with rapid loss of fluid in diarrhea, or with extensive necrosis in burns or acute injury of the liver, or in certain types of overwhelming infection. Apparently hyperguanidinemia is a result of secondary factors rather than an essential feature of any particular disease.

5. The intoxications seen clinically are in many respects similar to intoxication produced by experimental guanidine poisoning and are relieved in a similar manner by calcium therapy.

6. We believe that calcium medication is a valuable supplement to the common therapeutic measures employed in the management of such toxemias.

7. A method for the detection of guanidine-like substances in the blood is described.

Case Reports

GONOCOCCIC MENINGITIS IN A NEW BORN INFANT

WITH REVIEW OF THE LITERATURE

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Since Home,[1] in 1805, observed certain nervous manifestations associated with gonorrhea, occasional reports have appeared of gonococcic disease of the brain and meninges. The literature accumulated on this rare condition during the next hundred years was well reviewed in 1909 by Henderson and Ritchie.[2] The gonococcus was first discovered in 1879, and the differential sugar reactions and other methods of identification, such as agglutination, agglutinin absorption and complement fixation, were not introduced until 1905. It is quite obvious, therefore, that reports of cases before that time were based chiefly on clinical evidence. A gram-negative diplococcus isolated from purulent spinal fluid during the course of gonococcic infection within the urinary tract does not necessarily prove the organism to be the gonococcus. Meningococcic meningitis may easily appear in a patient suffering from gonococcic infection elsewhere. Moreover, Pick[3] cited an instance in which meningococcic infection of the seminal vesicles followed meningitis due to the meningococcus.

The criteria necessary to establish acceptable proof of the identity of the gonococcus are clearly presented by Birkhaug and Parlow[4] in their critical review of cases of gonococcic infection of the kidney. The organism should possess, in addition to the morphologic and cultural characteristics of the gonococcus, either the proper fermentation

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1. Home, Everard: Practical Observations on the Treatment of Strictures in the Urethra and in the Esophagus, ed. 3, London, W. Bulmer & Company, 1805, vol. 2, p. 211.

2. Henderson, G. and Ritchie, W. T.: Gonococcal Meningitis, Rev. Neurol. & Psychiat. **7**:75, 1909.

3. Pick, L.: Ueber Meningokokken-Spermatocystitis, Berl. klin. Wchnschr. **44**:947, 1907.

4. Birkhaug, K. E., and Parlow, A. L.: Gonococcal Infection of the Kidney, Jour. Urol. **20**:83, 1928.

Tabulation of Reported Cases of Gonococcic Meningitis Since 1905

No.	Author	Age	Sex	History	Termination	Autopsy	Source	Bacteriologic Data: Smear	Culture	Sugar Reactions	Agglutination	Complement Fixation	Comment
1	Wynn, W. H.: Lancet **1**: 352, 1905	24	M	Urinary tract infection; meningitis	D	+	Seminal vesicles; pelvic abscess; meninges	+ + 0	+ + 0	0 0 0	0 0 0	0 0 0	No organisms from the brain exudate
2	Prochaska, A.: Deutsches Arch. f. klin. Med. **83**: 184, 1905	19	M	Genital infection; meningitis	D	+	Blood; meningeal exudate	+ +	+ +	0 0	0 0	0 0	Not clearly differentiated from meningococci
3	Bieck, I. D.: Wratschebnaja Gazeta **14**: 1340, 1907	?	M	Chronic gonococcic urethritis for 1 year; meningitis	D	+	Urethra; meningeal exudate	+ +	0 0	0 0	0 0	0 0	
4	Romback, K. A.: Nederl. Tijdschr. v. Geneesk **2**: 1262, 1907	19	M	Acute meningitis 3 weeks after exposure to gonococcus	R	..	Spinal fluid	+	+	0	0	0	Bacteriologic study by de Josselin de Jong
5	Henderson and Ritchie: Rev. Neurol. & Psychiat. **7**: 75, 1909	23	M	Meningitis 8 days after urethral infection; suppurative arthritis of knee	R	..	Spinal fluid	+	0	0	+	+	Patient's serum (21st day) agglutinated gonococci but not meningococci
6	Morelli, F.: Riv. crit. di. clin. med. **12**: 533, 1911	?	M	Acute gonococcic urethritis; arthritis; meningitis	R	..	Urethra; spinal fluid	+ +	+ +	0 0	+	+	Patient's serum agglutinated organisms (1:60) but not meningococci
7	Boquet, H.: Le monde méd. **21**: 1066, 1912	26	M	Urethritis, cystitis, pyelonephritis, endocarditis; meningitis	D	+	Spinal fluid	+	+	0	0	0	
8	Boivin, M.: Bull. et mém. Soc. méd. d. hôp. de Paris **43**: 1024, 1919	25	M	Gonococcic urethritis; orchitis, arthritis, meningeal signs	R	..	Spinal fluid	..	0	..	..	..	No bacteriologic observations; cultures negative
9	Dundas, G. H. G.: Lancet **1**: 122, 1921	NB	?	Ophthalmia neonatorum; died tenth day; mother had vaginal discharge	D	+	Eye discharge	+	0	0	0	0	

10	Smith, D.: Lancet **1**: 1217, 1922	?	M	Acute urethritis; meningitis	D	0	Spinal fluid	+	+	+	+	0	Organisms not agglutinated by antimeningococcic serum
11	Schall, E.: Klin. Monatsbl. f. Augenh. **69**: 597, 1922	NB	?	Ophthalmia neonatorum; meningitis	D	0	Eyelid abscess; spinal fluid	+ +	0 0	0 0	0 0	0 0	
12	Lindenfeld, L.: Med. Klin. **18**: 176, 1922	53	M	Sepsis; meningitis; duration of illness 7 weeks	D	+	Seminal vesicles; spinal fluid	+ +	0 0	0 0	0 0	0 0	
13	Bruusgaard and Thjotta: Ann. de Dermat. **6**: 114, 1924	23	M	Sepsis; purpura; meningitis	R	..	Blood; spinal fluid; skin lesions	+ +	+	+	+	0	Organisms agglutinated by antigonococcic serum
14	Kroes, C. M.: Nederl. Tijdschr. v. Geneesk. **1B**: 1957, 1924	38	M	Typhoidlike illness; meningitis	R	..	Spinal fluid	+	+	+	0	0	Organisms at first considered to be meningococci
15	Giuliani, A.: J. d'urol. **20**: 415, 1925	60	M	Gonococcic infection of urinary tract; meningitis	R	..	.....	..	..	..	..	..	No bacteriologic observations
16	Hagi-Paraschiv and Nicolau; Bull. et mém. Soc. méd. d. hôp. de Bucarest **9**: 140, 1927	37	M	Genital infection; acute meningitis	R	..	Spinal fluid	..	0	..	..	..	Cultures negative
17	Lorentz, L.: Dermat. Wchnschr. **89**: 1305, 1929	30	M	Urethritis; arthritis; purpura; sepsis; meningitis	R	..	Spinal fluid	+	+	+	+	0	Organisms agglutinated by antigonococcic serum 1:200
18	Grenet et al.: Arch. de méd. d. enf. **33**: 731, 1930	7	F	Vulvovaginitis; sepsis; arthritis; purpura; meningitis	D	+	Blood; spinal fluid	+ +	+ +	+ +	+ +	0 0	Organisms not agglutinated by antimeningococcic serum
19	Weil, et al.: Bull. et mém. Soc. méd. d. hôp. de Paris **47**: 1799, 1931	20	M	Cystitis; meningitis	R	..	Spinal fluid	+	+	+	+	0	No agglutination by antimeningococcic serum
20	Coste et al.: Bull. et mém. Soc. méd. d. hôp. de Paris **47**: 1803, 1931	19	F	Metritis, 2 months' duration; arthritis of knee; meningitis	R	..	Spinal fluid	+	+	+	+	0	No agglutination by antimeningococcic serum

reactions or such serologic evidence as a positive complement-fixation or agglutination test. Of these tests, the characteristic sugar reaction (fermentation of dextrose only) would seem to furnish the most reliable evidence.

In this paper, an attempt is made to review the cases reported in the literature since 1905. In addition, we present the observations made in a case of gonococcic meningitis occurring in a new-born infant. Some cases reported in the literature are omitted because of inadequate studies, while others seem to emphasize various complications in the central nervous system such as encephalitis or myelitis rather than purulent meningitis. Since many of the reports of cases appear in the foreign literature, it is probable that a few definitely proved cases may have escaped our notice.

From the accompanying table, it is evident that only a few reports present authentic proof that the isolated organism was the gonococcus. The cases reported by Lorentz,[5] Smith,[6] Weil, Duchon and Bertrand,[7] Coste and his associates [8] and Pruusgaard and Thyotta seem to have been adequately proved. Those cited by Morelli,[9] Lindenfeld [10] and Kroes [11] would undoubtedly be acceptable to many.

As might be expected, the majority of the cases have occurred in adults during the course of genital infection or sepsis.

Two cases are reported in children. D'Amato [12] reported the case of a 2½ year old girl who died of meningitis following ophthalmia. The bacteriologic study was incomplete. The case of Grenet and Laurent [13] occurred in a 7 year old girl following gonococcic vulvovaginitis and disease of the joints and heart. The bacteriologic evidence was convincing.

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5. Lorentz, K.: Ueber Meningitis gonorrhoica, Dermat. Wchnschr. **89**:1305, 1929.

6. Smith, D.: Gonococcal Meningitis, Lancet **1**:1217, 1922.

7. Weil, Duchon and Bertrand: Méningite primitive à gonocoques traitée par un auto-lysat-vaccin, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:1799, 1931.

8. Coste, F.; Rivalier, E., and Layani, F.: Nouveau cas de méningite gonococcique, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:1803, 1931.

9. Morelli, F.: Contributo clinics allo studio delle localizzazioni meningee del gonococco di Neisser, Riv. crit. di. clin. med. **12**:533, 1911.

10. Lindenfeld, L.: Ueber Meningitis gonorrhoica, Med. Klin. **18**:176, 1922.

11. Kroes, C. M.: Etterige meningitis van ongewonen oosprong, Nederl. tijdschr. v. geneesk. **1B**:1957, 1924.

12. d'Amato, V.: Meningio encefalite gonococcica secondaria ad oftelmoblenorrea, Boll. d. mal. ven., sif. e d. pelle **1**:153, 1900.

13. Grenet, H.; de Pfeffel, Laurent, and Levent, R.: Vulvo-vaginite; septicemie, endocardite et meningite a gonococques, Arch. de méd. d. enf. **33**:731, 1930.

Only two cases of infection in the new-born, that of Dundas [14] and that of Schall,[15] are cited. This is not unusual in view of the relatively low incidence of any type of meningitis during that period of life. Holt,[16] Cook and Bell [17] and Barron [18] did not mention the occurrence of gonococcic meningitis in their discussions of meningitis in infants. Furthermore, Cooperman [19] reported sixty-seven cases of gonorrhea resulting from an epidemic in a nursery. Although fifty-three of these infants presented articular symptoms and fourteen had infections of the mucous membranes, there were no instances of meningitis and no deaths.

The case of Dundas,[14] although lacking in bacteriologic proof, suggests that the purulent meningitis found at necropsy was probably related to ophthalmia neonatorum. The course of clinical events was similar to that in our case.

Schall [15] cited the case of a new-born infant who died from meningitis following an orbital abscess. Smears from the abscess revealed gonococcus-like organisms, but the cultures yielded Staphylococcus aureus. Smears from the purulent spinal fluid also revealed gram-negative diplococci, but the cultures were negative. Permission for necropsy was denied.

It seems highly probable, therefore, that each of the aforementioned cases was an instance of gonococcic meningitis in the new-born, although the bacteriologic proof was not conclusive.

REPORT OF A CASE

History.—Baby G., a boy (3060 Gm.), was born on Aug. 1, 1932, by normal delivery after a labor of fifteen hours' duration. The position was left occipital anterior. The membranes ruptured four hours before delivery. The baby cried spontaneously. Crédé prophylaxis was carried out immediately after birth.

Examination.—Physical examination revealed a normal boy.

Course.—Two days after birth, ophthalmia neonatorum occurred in the right eye. Smears stained by Gram's method revealed many organisms resembling

14. Dundas, G. H. G.: Ophthalmia Neonatorum before Birth, Lancet **1**:122, 1921.

15. Schall, E.: Gonorrhoischer Lidabszess und tödliche Meningitis nach Gonoblennorrhöe eines Neugeborenen, Klin. Monatsbl. fur Augenh. **69**:597, 1922.

16. Holt, L. E.: Observations on Three Hundred Cases of Acute Meningitis in Infants and Young Children, Am. J. Dis. Child. **1**:26 (Jan.) 1911.

17. Cook, J. V. and Bell, H.: The Incidence of Meningitis in Early Infancy with a Description of 2 Cases Due to Unusual Organisms, Am. J. Dis. Child. **24**: 387 (Nov.) 1922.

18. Barron, M.: Meningitis in the Newborn and in Early Infancy, Am. J. M. Sc. **156**:358, 1918.

19. Cooperman, M. B.: Gonococcus Arthritis in Infancy, Am. J. Dis. Child. **33**:932 (June) 1927.

gonococci. This condition rapidly responded to local therapy, and the smears became negative within seven days.

On the sixth day of life, the patient became fretful and refused food. Nine days later, facial twitching was noted. Coarse nystagmus was evident. The temperature rose to 39 C. (102.2 F.). Definite enlargement of the joints in the toes and fingers occurred. The blood counts revealed: red cells, 3,500,000; hemoglobin, 75 per cent; white cells, 48,600, with 71 per cent polymorphonuclears.

On the eighteenth day of life, lumbar puncture confirmed the diagnosis of meningitis. The fluid was turbid and under increased pressure. There were 16,000 cells per cubic millimeter. Smears showed the cells to be chiefly polymorphonuclear leukocytes.

Treatment.—Because of the convulsive attacks the patient was treated by repeated lumbar punctures and by the injection of magnesium sulphate and sodium phenobarbital. Repeated ventricular and spinal taps were performed, and several injections of antimeningococcic serum were made. Later, generalized diathermy was tried on four occasions. The condition grew progressively worse, and death occurred on Sept. 10, the forty-first day after birth.

Autopsy.—Only the observations on the brain were significant. It weighed 550 Gm. Extensive subarachnoid hemorrhage was noted over the superior surface of both frontal lobes and the inferior surface of the cerebellum. Large accumulations of purulent exudate were found over the surface of the temporal lobes, the optic chiasm, and the cerebellum. The brain was very soft. After fixation, the left lateral ventricle was found to be markedly dilated. Each lateral ventricle and the third ventricle contained thick yellow exudate. The fourth ventricle was enormously dilated. Section of the cerebellum revealed extensive hemorrhages.

Bacteriologic Examination.—A direct smear (Gram stain) of the spinal fluid showed many intranuclear and extranuclear gram-negative biscuit-shaped diplococci. Cultures of the fluid on plain blood agar plates were negative. Cultures of the fluid on dextrose ascitic blood agar slants, under reduced oxygen tension, revealed in twenty-four hours a pure culture of gram-negative diplococci. Transferred to the differential sugar-ascitic agar tubes, the following fermentation reactions occurred: dextrose, acid; maltose, negative; lactose, negative; sucrose, negative. (On the same batch of sugars, a stock laboratory strain of meningococcus gave the following reactions: dextrose, acid, maltose, acid; lactose, negative; sucrose, negative.) On two other occasions, a specimen from the spinal fluid and one from the ventricular fluid were tested, with similar results.

The same type of organism was isolated from the meningeal exudate at autopsy.

Agglutination Reactions: On the thirtieth day of life, the patient's serum agglutinated a saline suspension of the organism in 1:40 dilution. A control serum taken from a person who had not had gonorrhea did not agglutinate this strain of gonococcus.

On the same day, a polyvalent antimeningococcus serum failed to agglutinate the organism.

An antigonococcic agglutinating serum was not available for study. Complement-fixation studies on the patient's serum were not made. Blood cultures, taken twice during the illness, were found to be sterile when cultivated on plain blood agar, enriched dextrose ascitic blood agar and in Douglas's broth.

Blood cultures remained sterile on three attempts.

Direct smears from the purulent optic discharge revealed intracellular and extracellular gram-negative diplococci. On one occasion, the culture yielded Staphylococcus albus and a few colonies of gram-negative diplococci. When grown

in pure culture, the latter organism gave the sugar reactions typical for the gonococcus.

Cultures for the gonococcus from the throat and nasopharynx were negative on two occasions.

A cervical culture from the mother yielded a gram-negative diplococcus, which in pure culture gave the typical sugar reactions for the gonococcus and was not agglutinated by polyvalent antimeningococcus serum.

COMMENT

Reviewing the case, the salient facts are as follows: In a new-born infant, normally delivered from a mother with gonococcic cervicitis, ophthalmia neonatorum developed on the second day. On the sixth day, generalized illness occurred, including fretfulness, fever, refusal of food and swollen red joints. On the eighteenth day, the diagnosis of purulent meningitis was established. An organism was isolated in pure culture from the spinal fluid which on further study gave the morphologic, cultural, fermentative and agglutinating characteristics of the gonococcus. The infant died on the forty-first day, and autopsy revealed purulent meningitis. The same organism was again isolated from the meningeal exudate.

In view of the clinical and bacteriologic evidence, the diagnosis of gonococcic meningitis would seem justified.

SUMMARY

An attempt is made to review the reported cases of gonococcic meningitis since 1905.

Definite bacteriologic proof is offered in only a few of the cases reported.

Only two instances of the disease occurring in the new-born are reported; each of these reports lacks complete bacteriologic proof that the etiologic agent was the gonococcus.

A third case of gonococcic meningitis in the new-born, in which we believe the diagnosis is adequately established, is presented.

AGRANULOCYTOSIS IN CHILDHOOD

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Agranulocytic angina as such was first described by Werner Schultz in 1922.[1] His primary concepts and his later acceptances[2] of variabilities, owing to the multiplicity of true cases reported, are too widely acknowledged to permit of repetition here. Neither Schultz nor his early followers seemed to admit the possibility of this syndrome occurring in childhood, though previous to his report some instances had been recorded. Schwartz[3] reported a case in a child in 1904, and Leale[4] presented a case in an infant with recurrent attacks of furunculosis associated with leukopenia. This case will be discussed in greater detail later.

Following the admission to the Long Island College Hospital of the patient whose case is reported in this paper, a review of the literature of agranulocytosis in childhood was made with the idea of charting and analyzing the cases to determine whether any could be classified as primary agranulocytosis or whether in the cases in childhood there are definite concurrent factors to account for the disappearance of the granular cells in the blood.

It was decided to omit from the table: (1) cases in which there were a high white cell count with increased relative lymphocytosis, for in these the shadow of leukemia presents itself; (2) cases in which there are acknowledged concurrent acute infections, such as pneumonia or typhoid with leukopenia; (3) cases in which antisyphilitic treatment has

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1. Schultz, W.: Ueber eigenartige Halserkrankungen und Defekt des Granulozytensystems, Deutsche med. Wchnschr. **48**:1495, 1922.

2. Schultz, W., and Jacobowitz, L.: Bemerkungen zur Arbeit von Julien Weiss: Ueber die gegenseitungen Beziehungen zwischen Schultzschen Symptomen-Komplex (Mucositis necroticans agranulocytica) akuter Leukämie, und septischer Infekt, Wien. Arch. f. inn. Med. **15**:205 (Feb.) 1928.

3. Schwartz, E.: Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. **3**:190, 1904.

4. Leale, M.: Recurrent Furunculosis in an Infant Showing an Unusual Blood Picture, J. A. M. A. **54**:1854 (June 4) 1910.

been administered (these have been admirably reviewed by Farley,[5] and Dodd and Wilkerson[6]); (4) cases in which there is definite diphtheritic involvement (Farmakides[7]); (5) cases in which previous deep roentgen exposures had been administered, and (6) cases in which the patient had ingested known poisons such as benzine.

In the table no attempt at classification has been made.

ANALYSIS OF TABLE

Age.—The youngest patients whose cases were reported were infants 10 weeks and 12 weeks of age, respectively. Both of these children recovered.

Sex.—In the thirty cases reported neither sex showed a predominance.

Preceding Symptoms.—With only four exceptions, all of the patients whose cases are reported had definite histories of immediate antecedent acute infections leading up to the period of agranulocytosis. Of the exceptions, in case 6 there was an acute onset with sore throat, fever and anorexia, associated with marked agranulocytosis and sepsis. This child died in ten days. In case 8 the history did not account for the sudden onset. A plaque appeared on the tonsil, which was proved to be nondiphtheritic. The child died in five days with grave agranulocytosis. The patient in case 10 is at present a young adult who has been observed for a period of twenty years; in this case, the original inception was leukopenia associated with furunculosis. The patient in case 11 (b) had had pneumonia three months previous to her admission, but afterward had been well. The attack in this case was fatal; it lasted only ten days.

Studies of the Blood.—Anemia was a pronounced factor in all of the cases, with only one exception. There was, too, a marked reduction of the red cells, with agranulocytosis and leukopenia. All but four patients had 10 per cent or less of the granulocytic element at least at one time during their illness. Twenty-six cases showed 5 per cent or less. Platelet counts were not invariably reported and were not constant.

Cultures of the Blood.—Nine patients had septicemia. The organism recovered was not constant, though Staphylococcus aureus-haemolyticus predominated. Many of the others by their courses suggested the presence of bacterial invasion of the blood.

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5. Farley, D. L.: Depressed Bone-Marrow Function from Arsphenamine, Including Type of So-Called Agranulocytosis, Am. J. M. Sc. **179**:214 (Feb.) 1930.

6. Dodd, K., and Wilkerson, S. J.: Severe Agranulocytic Aplasia of Bone Marrow, J. A. M. A. **90**:663 (March 3) 1928.

7. Farmakides, C.: De quelques cas d'agranulocytose au cours de la diphtérie, Presse méd. **37**:1121 (Aug. 28) 1929.

Table Showing D... rted in Ca...

Case	Reference	History*	Age and Sex	Red Cells	Hemoglobin, per Cent	White Cells	Polymorphonuclears, per Cent	Small Lymphocytes, per Cent	Monocytes, per Cent
1	Schwartz, E. (Mitt. d. Gesellsch. f. inn. Med. und Kinderh. **3**: 190, 1904)	Abscess of the kidney immediately preceding admission	9 yrs., female	.....	..	600	..	100	..
2	Bantz, R. (München. med. Wchnschr. **72**: 1200 [July 17] 1925)	10 weeks of illness associated with fever	4½ yrs., male	3,900,000	35	6,700 2,300	0	92	..
3	Weiss, J. (Wien. Arch. f. inn. Med. **14**: 303 [May] 1927)	Upper respiratory infection and otitis media 14 days before onset	6 yrs., male	4,200,000	60	3,300 1,100	1	80	18
4	Carrau, A. (An. Fac. de med., Montevideo **13**: 70 [Jan.] 1928)	3 months previous to admission had sore throat and tonsillitis	3 yrs., male	.....	..	4,800	6	86	..
5	Durger, H. L., and Helwig, F. C. (Am. J. Dis. Child. **35**: 1041 [June] 1928)	Mikulicz syndrome, 4 months previously; toothache and gingivitis immediately preceding admission	6 yrs., male	2,600,000	..	11,800 2,800	12 0	88 100	..
6	Dayton, C. M. (Northwest Med. **27**: 436 [Sept.] 1928)	Sudden onset, with sore throat fever, anorexia, hemorrhage, gingivitis and nasal hemorrhage	7 yrs., female	3,000,000	..	600	2	98	..
7	Christof, N. (Wien. klin. Wchnschr. **42**: 335 [March 14] 1929)	Pyodermia 2 weeks postnatal; 3 weeks later hemorrhagic gastro-enteritis lasting 2 weeks	3 mo., male	.....	..	4,800	2	76	22
8	Dufourt, M. A. (Lyon méd. **141**: 679 [June 10] 1928)	Child well up to 1 month before onset, when gastric upset occurred	12 yrs., female	2,050,000	50	1,230	10	29	60
9	Tokué, K., and Vasumato, M. (Am. J. Dis. Child. **38**: 1037 [Nov.] 1929)	Osteomyelitis one month previous to admission	4 yrs., male	1,896,000	24	800	0	100	..
10	Rutledge, B. H.; Hansen-Prüss, O. C., and Thayer, W. S. (Bull. Johns Hopkins Hosp. **46**: 369 [June] 1930)	Recurrent attacks of agranulocytosis since 10 weeks of age	2½ mos. to 20 yrs., male	Normal	Normal	Diminished	..	66	..
11(a)	Jacobsen, A. W. (Canad. M. A. J. **22**: 814 [June] 1930)	Previous history of petechiae appearing over body	18 Mos., female	1,170,000	19	3,400	8	90	..
(b)		Pneumonia 3 months previous to admission	4 yrs., female	.....	..	1,200	5	95	..
12(a)	Bigler, J. A., and Brennemann, J. (Am. J. Dis. Child. **40**: 515 [Sept.] 1930)	2 months previously, tonsils and adenoids removed; pains in wrists and shoulders for 1 month	7 yrs., female	1,700,000 (average)	30	2,500 (lowest)	2	96	..
(b)		2 months of listlessness, with 1 month of irregular temperature, associated with weakness	6 yrs., female	1,100,000 (average)	20	2,010	1	97	..
(c)		Pain present over hips and spine associated with rise in temperature	11 yrs., female	870,000 (average)	..	1,300 (average)	2	98	..
(d)		6 weeks before onset acute pain in legs and elbows; 2 weeks previously, black and blue spots over body	5 yrs., male	2,000,000	..	4,000	6	89	..
(e)		8 weeks of loss of appetite and pallor; 3 days previously petechiae and fever	2 yrs., male	1,500,000	40	1,640	..	100	..
(f)		6 weeks of increasing pallor and weakness	3½ yrs., male	2,200,000	50	825	6	94	..
(g)		4 months before admission, severely ill; 3 days before onset had acute upper respiratory infection	6 yrs., female	4,000,000 1,200,000	40	4,700 1,200	21 12	76 86	..
(h)		Ill 6 days before admission	3½ yrs., female	2,200,000	20	1,300	4	96	..
(i)		Otitis media of right ear 4 months before admission	3½ yrs., male	2,100,000	20	1,300	4	96	..

Small Lymphocytes, per Cent	Large Lymphocytes, per Cent	Monocytes, per Cent	Basophils, per Cent	Platelets	Culture of the Blood	Duration and Terminus	Notes and Treatment
100	..	..	...	.....	.....	9 days; died	
92	8	..	...	.....	.....	Died	On autopsy there was a definite gangrenous involvement of the throat and pharynx
80	..	18	...	.....	.....	2 to 3 wks.; died	Treated with neoarsphenamine locally and intravenously; lesion in throat
86	6	..	...	.....	.....	3 mos., died	Child was ill and listless since illness 3 months before onset
88 100	..	..	...	.....	At autopsy, Strep. viridans recovered	Died	Child developed agranulocytosis—then appeared to be doing well; tooth extracted, and patient died 2 days later; blood count returned to normal during interim; treatment by weekly transfusions of blood, injections of sodium perborate, U. S. P., given locally
98	..	..	...	Diminished	Strep. viridans	10 days; died	Showed black sloughing crusts on lips with necrosis of gums; teeth loose; given citrated blood and finally transfusions of whole blood
78	..	22	...	.....	.....	Approximately 2 wks.; recovered	Treated with injections of acriflavine hydrochloride and a nonspecific substance containing albumin, lipoid and fat; mild mercurous chloride given by mouth
39	..	60	...	.....	.....	5 days; died	Plaque on tonsil; child suddenly became sick. Because of plaque treated for diphtheria; cultures negative, however, patient died in 5 days
100	..	..	...	584,000	.....	7 days; died	Grayish membrane over tonsil; cutaneous eruption present
66	32	..	0.2	Diminished in attack	.....	Recurrence every 3 wks.	Started with recurrent attacks of furunculosis with agranulocytosis; later lesions appeared in mouth and gums; attacks recur every 3 weeks
90	2	..	...	.....	.....	3-4 wks.; died	Child seemed to be recovering, then experienced an attack of pneumonia and died
95	..	..	...	.....	.....	10 days; died	Ulcerations over pharynx, associated with questionable thoracic effusion
96	..	..	...	Reduced	Staph. aureus	Died	Autopsy showed absence of granular cells in the marrow
97	..	..	...	.....	Staph. aureus	Died	Gums ulcerated—oozing blood; petechial hemorrhages about the legs with ecchymoses about the ankles
98	..	..	...	.....	.....	2 mos. after admission; died	Four weeks after admission, petechiae appeared over the body; temperature fluctuated between 101 and 105 F.
89	..	..	...	82,000	.....	11 days after admission; died	Child had septic course
100	..	..	...	.....	.....	6 days after admission; died	Child had septic course; petechiae appeared over body
94	..	..	...	.....	.....	Died	Child had septic course; petechiae appeared—hemorrhage from gums and lips
76 86	..	..	...	Diminished	.....	2 days after 2d admission; died	Child recovered from first infection; readmitted several days later with history of pallor for 4 weeks; 2 weeks later sore throat; petechiae over body, septic temperature
90	..	..	...	.....	.....	7 wks. after onset; died	Child had septic condition; temperature between 101 and 103 F.; purpuric spots appeared on extremities, with hemorrhagic areas about one ear
96	..	..	...	.....	Staph.; septicemia on autopsy	17 days after admission; died	Septic temperature two days before admission; petechiae appeared over the body, with hemorrhage into the retina

Case	Reference	History*	Age and Sex	Red Cells	Hemoglobin, per Cent	White Cells	Polymorphonuclears, per Cent	Large Mono...
13(a)	Baldridge, C. W., and Needles, R. J. (Am. J. M. Sc. **181**: 533 [April] 1931)	10 days before admission, grayish membrane about the nose; on admission, glandular enlargement	8 yrs., female	3,660,000	90	600	5	
(b)		11 days before onset, sore throat; 2 days before admission, tooth extracted	7 yrs., male	830,000	25	3,100	8 2	
14	Hyde, C. I. (Arch. Pediat. **47**: 404 [June] 1930)	4 weeks previous to admission, swelling of right side of face in front of ear	4 yrs., male	2,010,000	..	2,200 750	22 0	
15(a)	Dameshek, W., and Ingall, M. (Am. J. M. Sc. **181**: 502 [April] 1931)	Acute upper respiratory infection before admission, with subsequent pneumonia	16 mos., female	5,100,000	..	5,500	0	
(b)		Otitis media of the right ear, 6 to 12 weeks before admission, with recurrence 10 weeks previously	2½ yrs., male	1,900,000 1,300,000	50 38	3,600 6,800	0 0	
16	Raillet, M. M., and Ginsbourg, H. (Bull. et mém. Soc. méd. d. hôp. de Paris **54**: 1318 [July 21] 1930)	Purulent arthritis for 1 month with epidemic icterus; purpura 3 months previously	10 yrs., male	3,900,000	80	1,600	6	
17	Harkins, H. N. (Arch. Int. Med. **47**: 408 [March] 1931)	Sore throat, inanition and lassitude for 1 week	2 yrs., female	890,000 2,600,000	45	3,600 850	8	
18	Connors, H. M., and co-workers [17] Proc. Staff Meet., Mayo Clin. **6**: 193 [April] 1931)	6 weeks previous to admission, weakness and anorexia marked	4 yrs., female	860,000	10	4,000 1,000 700	18 14 10	
19	Givan and Shapiro (case reported in this paper)	4 months of otitis media; rash appeared over body 1 month previously, followed by 4 days of acute fever immediately before admission	7 yrs., male	.....	40-50	600	0	

* The time element refers to days previous to admission to the hospital.

Lesions.—Lesions were not constant, but when present were in the buccal region and varied from the formation of plaques on the tonsils to ulcerative gangrenous processes of the pharynx.

Duration.—The duration varied; sometimes it was as short as four days, and sometimes the condition lasted two months.

Autopsy Reports.—The reports showed universal involvement of the bone marrow granular cell centers. Three of the cases presented by Brennemann and Bigler came to autopsy, and the observations disproved aplastic anemia suggested by the cell counts of the peripheral blood.

Recurrences.—One patient has had recurrences. He has been the subject of close observation for twenty years by competent physicians. The case was first reported by Leale [4] as was previously mentioned. He is prone to attacks every three weeks. At first he presented a picture of leukopenia associated with furunculosis; then, following the use of an autogenous vaccine, the furunculosis disappeared, but the occurrence of leukopenia associated with agranulocytosis continues regularly. Occasionally, there is some membranous involvement of the tonsillar region. The attacks begin and end spontaneously.

ata Re… Cases—Continued

Poly-morpho-leucocytes, per Cent	Large Lymphocytes, per Cent	Monocytes, per Cent	Basophils, per Cent	Platelets	Culture of the Blood	Duration and Terminus	Notes and Treatment
5	1	5	...	.....	Staph. aureus and B. typhoid	23 days; died	Nine days after admission ulceromembranous stomatitis developed, with petechiae over body; on autopsy typhoid organisms found
8 2	..	..	...	.....	B. coli; 2 days ante mortem	Died	Cervical glandular enlargement present; membrane appeared over the left tonsil; eight transfusions of blood given
22 0	..	7	...	.....	Staph. aureus	Died	Extreme pallor and prostration present; condition ran septic course
0	0	..	...	.....	.....	14 days; recovered	Blood picture at first that of complete agranulocytosis; with release of sepsis normal count appeared
0 0	..	..	...	.....	.....	6 days; died	Autopsy revealed presence of myeloblasts in bone-marrow; patient treated with transfusions
6	..	28	...	.....	Meningococcus	Died	Septicemia present following what may have been septic infection 3 months previously
8	..	4	...	90,000	.....	Died	Treated with three intraperitoneal transfusions and 20 cc. of a nuclear extract given every 4 hours for 4 days; child recovered to return in 2 months and die of sepsis
18 14 10	..	..	...	128,000	.....	Died	Treated with transfusions of blood; a cellulitis developed in the region of the jaw; membranous exudate present over the tonsils
0	3	..	...	Normal	Staph. aureus	Recovered	Treated with infusions of adenine sulphate

Death.—Twenty-six of the thirty patients died.

Treatment.—The methods of combating the illness varied widely. Transfusions seemed to be employed predominatingly. The futility of the usual means employed in children is reflected in the mortality reports.

REPORT OF CASE

History.—V. de P., a boy, 7 years of age, was admitted to the Long Island College Hospital on June 4, 1931, because of septic temperature and swelling of the face of four days' duration. The illness began in March, 1931, starting with a bilateral purulent otitis media with a discharge during varying periods throughout the course. One month before admission an unexplained rash appeared over the body; it was most marked about the surfaces of the joints and was associated with a high temperature. The rash and the temperature lasted for four days and then cleared up spontaneously. Thereafter, the parents noted that the child was not so active as he had been formerly. Four days prior to his admission to the hospital a temperature of 105 F. suddenly developed. At this time the gums were found to be bright red, spongy and swollen. In addition, there was a foul and fetid odor to the breath. The condition of the mouth became worse, and the temperature remained at from 104 to 105 F. He was seen then by one of us (T. B. G.) for the first time and immediately sent to the hospital.

Physical Examination.—Physical examination revealed an acutely ill and toxic boy. The face was pallid and puffy. There was a scant discharge from the left ear, and the right ear drum appeared to be bulging. On both of the inner surfaces of the cheeks, more pronounced on the left, were several small punched-out ulcerative areas, which were the size of a split pea. They were lined with a dirty grayish exudate, and were surrounded by necrotized tissue. The entire left cheek felt brawny and indurated.

The gums were spongy and bright red, bleeding at the slightest manipulation. The edges of the gums above the teeth were ulcerated and retracted. Many of the teeth were loose. The hard and soft palates were slightly edematous, and they were covered by a russet-colored, mucelloid material. The tongue was boggy and hard; it seemed to prevent the closure of the jaws. The child was unable to talk. The tonsillar region as far as could be seen was not involved, except for slight hyperemia.

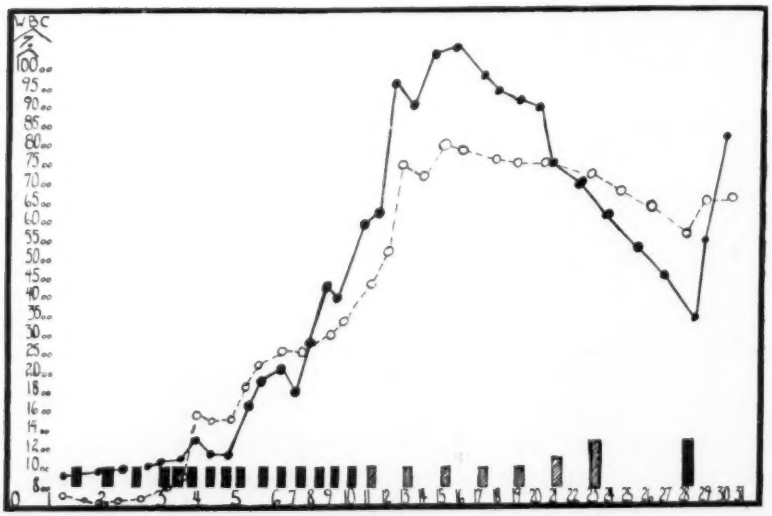

Chart showing the response of the white cells (continuous line with solid dots) and polymorphonuclear granulocytes (interrupted line with hollow dots) to the infusions of adenine sulphate (solid black columns) and transfusions of blood (columns with diagonal lines). The abscissae represent days in the hospital.

The breath was exceedingly foul. There was, too, a continuous oozing of blood-tinged saliva. Other than a slight enlargement of the anterior and posterior chains of cervical glands, the remainder of the physical examination gave negative results.

Course.—On the evening of admission to the hospital myringotomy was performed on the right side. No pus was liberated; only bloody serum. The same evening 0.3 Gm. of adenine sulphate in a saline solution was given intravenously with 500 cc. of dextrose. In this manner the adenine sulphate was administered twice the second day, three times the third day, twice the fourth and the fifth days and thereafter but once a day until the tenth day of his stay in the hospital.

On the fifth day intense jaundice developed. Both the liver and the spleen became palpable. The icteric index rose to 27.8; the van den Bergh test was positive in the indirect phase. The administration of adenine sulphate was not

discontinued when jaundice appeared, and after three days of rigorous administration of a hypertonic dextrose solution, the icterus cleared. Throughout the first weeks the stools were positive for occult blood, secondary to the oral condition.

Cultures of the gums and of the ulcerative areas of the cheeks showed pure growths of Vincent's organisms. Cultures of the tonsillar region were positive for the hemolytic streptococcus. The first two cultures of the blood, one taken on admission and one two days later, were positive for Staphylococcus aureus-haemolyticus; thereafter, they were sterile.

Twelve days after admission an abscess developed over the angle of the right mandible. The edges were dark blue, and a fluctuant crater-like area appeared in the center. This was incised, and a slight amount of green, foul-smelling pus was freed. A communicating sinus developed at the site of the incision, which drained food and saliva for weeks.

On the eleventh day after admission, after the total white cell count had risen to 9,800, with 76 per cent polymorphonuclear granulocytes, a small transfusion of 120 cc. of blood was given. Thereafter every other day over a period of two weeks a transfusion of like volume was administered. The hemoglobin did not rise sufficiently, however, and a final transfusion of 250 cc. was given.

Five days after the last transfusion was administered, the total white cell count had dropped to 3,400, with 61 per cent polymorphonuclears, and 0.5 Gm. of adenine sulphate was again administered. Twelve hours later, the white cells had risen to 6,250, of which 68 per cent were granular cells. Twenty-four hours later, the white cells numbered 8,400, with 68 per cent granular cells.

Throughout this period the temperature remained unaltered, fluctuating between 103, 104 and 99 F. Roentgenograms of the maxillae and the mandibles showed definite osteomyelitis of both bones.

Operation.—On July 20, Dr. E. J. Browder removed the entire sequestrated portions of both maxillae and mandibles, excising at the same time the entire left ramus of the mandible. Four days later the right ramus of the mandible from the angle to the symphysis was freed, and curettage of the alveolar sockets was performed.

This completed the débridement of the mouth. Only three teeth remained, two incisors and one canine, which were on the left side. With this operation the temperature subsided, and the child progressed to an uneventful convalescence. Up to the time of writing, ten months later, there has been no recurrence.

Laboratory Data.—Tests for kidney function and chemical examination of the blood gave negative results. During the height of the pyrexia, albumin appeared in the urine. A Wassermann test of the blood was negative, and bleeding and coagulation times, clot retraction, platelet counts and fragility tests were normal.

Local Treatment.—Potassium permanganate, sodium perborate and 10 per cent solutions of neoarsphenamine were applied locally. The intravenous injections of neoarsphenamine, given after the administration of adenine sulphate was discontinued, did much to clear up the superficial oral infection.

COMMENT

For three months previous to the attack, the child had an involvement of the ears and throat, which left him weakened. One month previous to his admission there appeared an unexplained rash over the body, most marked about the extensor surfaces of the joints. There-

after the weakness and listlessness were more accentuated until four days prior to admission, when the present illness began.

In view of the work done by Marzullo [8] at the Long Island College Hospital, based on the experience of Doane [9] and his co-workers and of Reznikoff,[10] it was decided to attempt nucleotide therapy to the exclusion of all else. Transfusions were interdicted because of their depressing action on the bone marrow.

Adenine sulphate, 0.3 Gm., in physiologic solution of sodium chloride was given, as indicated in the chart, for a period of ten days, while determinations of the peripheral blood cells were made every eight hours. Once the bone marrow showed its response and the total white cell count with the percentage of granular cells had reached its indicated level, the administration of adenine sulphate was discontinued, and small transfusions of 120 cc. were administered every other day for ten days to support the patient and to combat the anemia.

It is of interest to note that particularly after the last two transfusions, which were of greater quantity, 150 cc. and 250 cc. respectively, there was an alarming drop both in the total number of white cells and in the percentage of granular cells; again 0.5 Gm. of the adenine compound was administered, with good results.

CONCLUSIONS

The cause of this pathologic condition is not known. Numerous hypotheses have been presented. Rosenthal [11] summarizes the most probable ones as follows:

1. The condition is a specific disease entity.
2. It is a granuloleukopoietic disease of the bone marrow.
3. Some specific selective toxic action on the bone marrow is present, making the body less resistant to secondary invasion of bacteria.
4. The condition is due to an infection on a preexisting hypoplasia of the granulopoietic apparatus.
5. It is a malignant leukopenia of a leukemic nature.
6. The condition is secondary to an endocrine dyscrasia.
7. It is an atypical form of sepsis.

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8. The adenine sulphate was administered under the direction of Dr. Marzullo. Marzullo, E. M.: Personal communication.

9. Doane, C. A.; Zerfas, L. G.; Warren, S., and Ames, O.: Studies of Mechanism of Nucleinate Induced Leucopenic and Leukocytic States, J. Exper. Med. **47**:403 (March) 1928.

10. Reznikoff, P.: Nucleotide Therapy in Agranulocytosis, J. Clin. Investigation **9**:381 (Dec.) 1930.

11. Rosenthal, N.: Observations on Agranulocytosis, New York State J. Med. **30**:695 (June 15) 1930.

Rosenthal, himself, however, believes "it to be a clinical entity related to a constitutional hypoplasia of the leukopoietic system. The septic manifestations are of a secondary nature and produce pathological lesions which are common to septic conditions without the inflammatory reaction."

Of the various theories, the one recently presented by Hamburger [12] based on the works of Friedemann,[13] Roberts and Kracke,[14] and Rutledge and his associates [15] seem to us most acceptable.

> The primary disorder lies in a depressed function of the granulocytic mechanism of the bone-marrow with consequent agranulocytic leukopenia. Thereupon develops the lack of defense against infection which we have many reasons to believe the polymorphonuclear leukocyte in part affords. The cause of the defect in the leukopoietic system is totally obscure.

The age variation between the series described here and those previously mentioned does not necessarily limit their interrelationship.

In twenty-six of the thirty cases here presented there was a definite antecedent infection. In some of the cases in adults reviewed by Rosenthal [11] there were histories of infections previous to the stage of agranulocytosis. Hamburger,[12] however, reported that not one case of his series was preceded by any known illness. However, until the influence of different infections on the bone marrow is more clearly understood, the comparative rarity of infection in childhood associated with leukopenia being kept in mind, the cases here presented must be classed as a unit. Until more fully understood reports are given, such as have been presented by Roberts and Kracke [14] and Rutledge,[15] the true classification must be deferred.

Bigler and Brennemann [16] stated that they believe the disease to be "a clinical entity characterized by gradual onset, fairly short course with fatal termination, fever, severe anemia, petechial hemorrhages with a low platelet count, and leukopenia with a decrease in granulocytic cells." Connors [17] and his associates sought to differentiate between agranulocytsois and hypogranulocytosis. We agree with Hamburger,[12] to wit:

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12. Hamburger, L. P.: Treatment of Agranulocytosis, Bull. Johns Hopkins Hosp. **48**:339 (May) 1931.

13. Friedemann, U.: Angina with Extreme Leukopenia, Med. Klin. **19**:1357, 1923.

14. Roberts, S. R., and Kracke, R. R.: Agranulocytosis, J. A. M. A. **95**:780 (Sept. 13) 1930.

15. Rutledge, B. H.; Hensen-Prüss, O. C., and Thayer, W. S.: Recurrent Agranulocytosis, Bull. Johns Hopkins Hosp. **46**:369 (June) 1930.

16. Bigler, J. A., and Brennemann, J.: Sepsis with Leukopenia (Agranulocytosis) in Children, Am. J. Dis. Child. **40**:515 (Sept.) 1930.

17. Connors, H. M.; Margolis, H. M.; Birkeland, I. W., and Sharp, J. E.: Agranulocytosis and Hypogranulocytosis, Proc. Staff Meet., Mayo Clin. **6**:193 (April) 1931.

"A condition approaching nosologic chaos is created by the fact that the term agranulocytosis has been transferred from the original meaning assigned to it by Werner Schultz." [1]

This review has shown that cases simulating the accepted form of primary agranulocytosis do occur in children. Four true instances of this are seen in cases 6, 8, 10 and 11 (b) in the accompanying table. However, aside from the sharp inception, these four cases vary little, if at all, from the others.

The question of recurrences as a distinguishing mark between so-called primary and secondary agranulocytosis cannot be answered here, for twenty-six of the thirty patients died in the initial attack. Of the four survivors, one child is having cyclic recurrences, as has been previously mentioned; in the other three no recurrence has been reported.

The presence of septicemia cannot be a differential factor, for, to mention a few instances, both Rosenthal [11] and Hamburger [12] presented cases of proved septicemia in their series. In Roberts and Kracke's case septicemia developed after the agranulocytosis had become marked. The child whose case has been reported in this paper had organisms in the blood stream but the cultures of the blood became sterile coincidently with the rise in the number of granular cells.

SUMMARY

Twenty-nine cases of agranulocytosis in childhood are reviewed, and an additional case is added.

The instances of agranulocytosis in children with severe antecedent infection must be regarded as a unit.

Finally, a case is presented in detail in which antecedent infection was marked and agranulocytosis was superimposed. Adenine sulphate was used to stimulate the marrow centers, with good results, for with the reappearance of the granular elements, the peripheral blood stream, from which Staphylococcus aureus-haemolyticus had previously been recovered, became sterile. Of note is the fact that when transfusions were started there was a coincident drop in the total number of white cells and in the percentage of granular cells. One injection of adenine sulphate, however, was sufficient to cause a return of the cellular elements to their previously attained level. The patient was then able to withstand two radical operations on the jaw, and recovery was uneventful.

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CARCINOMA OF THE SKIN IN CHILDHOOD

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Neoplasia occurring in infancy and in childhood is comparatively rare. Of the systems involved the skin is a common site. Philipp,[1] in a review of the literature, collected sixteen cases, comprising 17 per cent of all types of malignancy. In eleven of these cases, the growths developed on the basis of xeroderma pigmentosum, one subsequent to trauma of an old scar resulting from a burn, and the remainder, spontaneously. The majority of the growths were squamous cell carcinomas; in Williams' case, the growth was a basal cell type. Kondo[2] reported a case of squamous cell carcinoma in a 12 year old boy, originating in the skin of the hand and causing death by generalized metastases to the bones. In his review, Merkel[3] added the reports of six more cases, five of Rieder's and one of Vidal's; all the patients were boys less than 15 years of age, and members of the same families as those of the authors' previous patients. In Martinotti's[4] patient, a girl 12 years old, a cystic adenoid epithelioma of the thigh developed following trauma. In an 11 year old child, whose case was reported by Roth,[5] carcinoma developed at the site of an injury from a thorn. Dollinger[6] reported a case in a child under 15 in whom the condition developed on the basis of lupus vulgaris. A similar case was reported by Iredell[7] in a 13 year old boy who had had a tuberculous lesion of the skin for eleven years, and who had been subjected to roentgen therapy; a histologic description, however, is lacking. The case of

From the Pathologic Laboratory, City Hospital, Welfare Island, Department of Hospitals.

1. Philipp, P. W.: On Carcinomas of Childhood, Ztschr. f. Krebsforsch. **5**: 326, 1907.

2. Kondo, K.: Ein Hautkrebs mit generalisierten Knochenmetastasen im Kindesalter, Inaug. Dissert., Greifswald, H. Adler, 1909.

3. Merkel, H., in Brüning and Schwalbe: Handbuch der allgemeine Pathologie und der pathologischen Anatomie des Kindesalters, Wiesbaden, J. F. Bergmann, 1912, vol. 1, p. 417.

4. Martinotti, L.: A Single Observation of a Cutaneous Benign Epithelioma in a Twelve Year Old Girl, Gior. ital. d. mal. ven. **63**:198, 1922.

5. Roth, quoted by Follmann, J.: Cancer of the Skin in Children, Orvosi hetil. **71**:700, 1927.

6. Dollinger, quoted by Follmann.[5]

7. Iredell: Epithelioma on Lupus Vulgaris in a Girl of Thirteen, Brit. J. Dermat. **23**:246, 1911.

Follmann,[8] in which a tumor developed subsequent to trauma, is likewise doubtful.

The case to be reported is a further example of carcinoma of the skin in childhood. A striking feature was the high degree of histologic malignancy and the apparently benign clinical course.

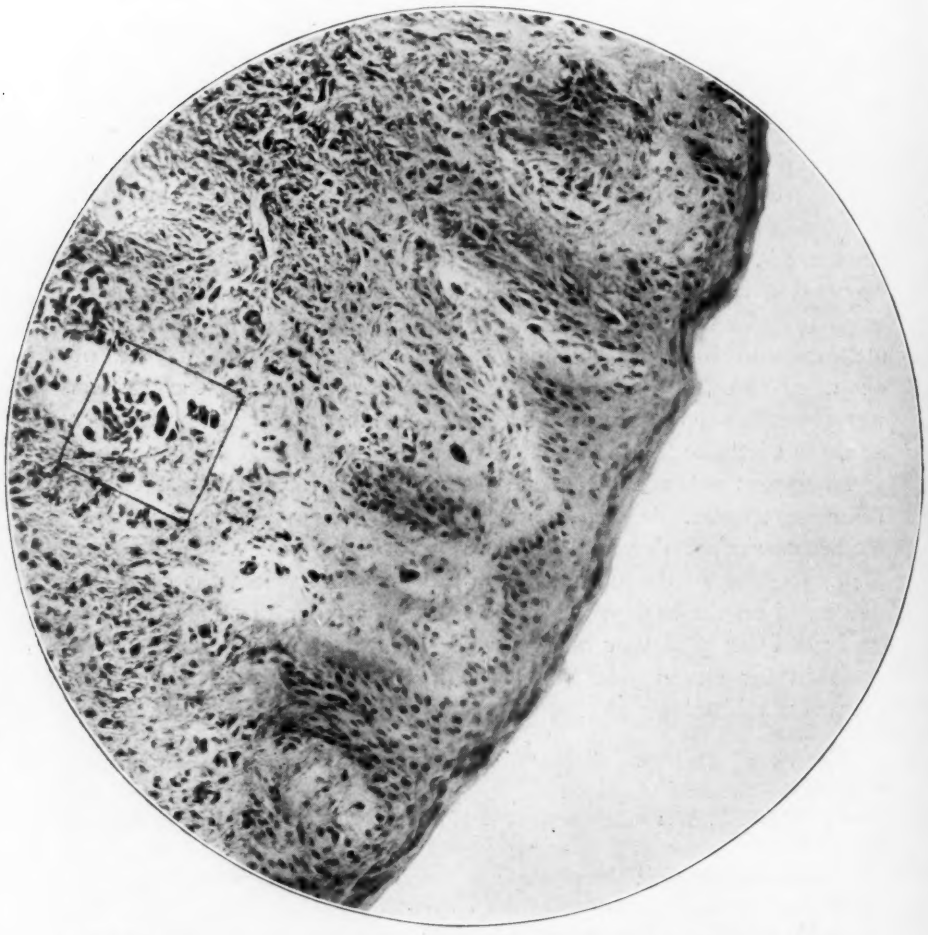

Fig. 1.—Low power photomicrograph. The disorganization of the rete pegs is marked and widespread. The darkly stained masses are individual cells. Nests of malignant cells are scattered diffusely through the central core.

REPORT OF A CASE

A boy, 10 years of age, of Polish parentage, was brought to the outpatient department of the City Hospital because of a pedunculated mass on the left side of the lower lip about 2 cm. below the mucocutaneous border. It had first appeared about six months previously as a pinhead-sized, cherry red, hard growth, and it

8. Follmann.[5]

had gradually grown to the size of a pea. During the few weeks prior to examination it bled easily on slight trauma. At no time was it painful, nor was there any known preceding injury.

There was no history of xeroderma pigmentosum or malignancy either in the maternal or the paternal progenitors. The mother had several small pigmented

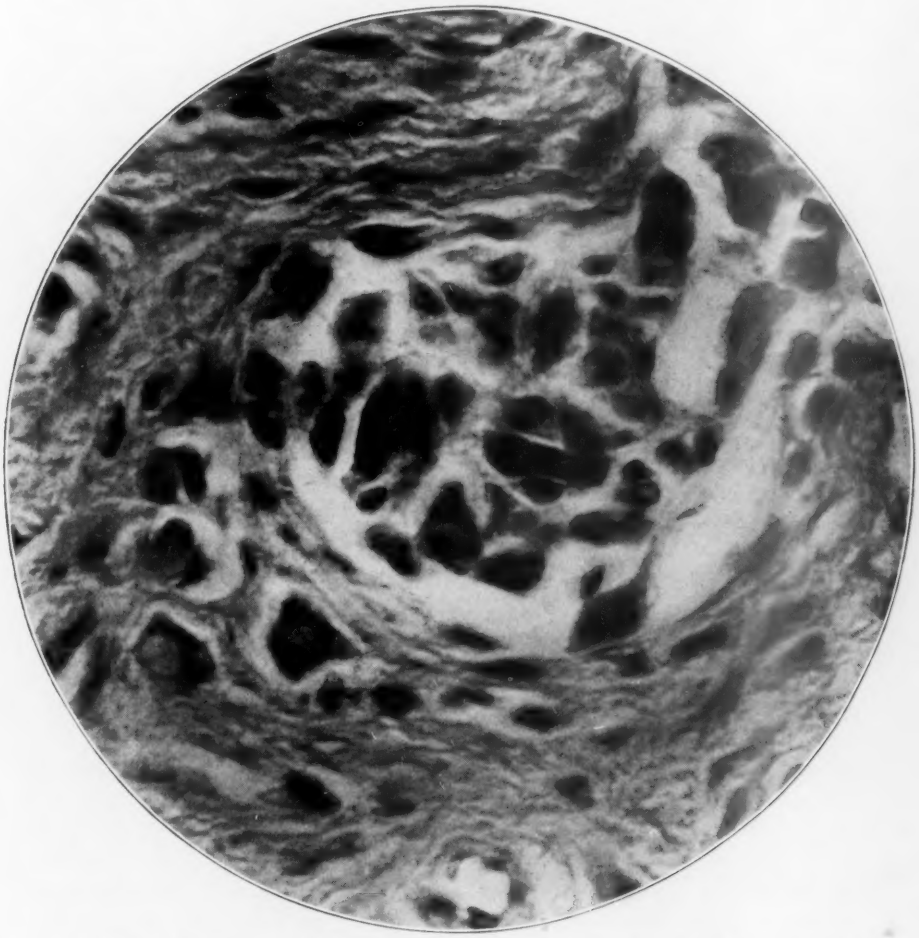

Fig. 2.—High power photomicrograph of the portion outlined in ink in figure 1. There is a malignant embolus within a lymphatic channel.

moles of the face and neck; the eldest son, a year older than the patient, manifested the same tendency. A younger son, 8 years old, had a clear skin.

Pathologic examination showed that the specimen consisted of a small pea-sized tumor, apparently completely covered by skin, with a dense fibrotic center and the gross appearance of a hard fibroma. Histologic examination revealed that the tumor was covered by thin squamous epithelium. The rete pegs displayed a great tendency toward downward growth and branching, the cells at the tip being large,

irregular and unequal, and the nuclei hyperchromatic and the basement membrane being absent. Between the pegs the epithelium was normal. Throughout the dense fibrous core were scattered, individually and in nests, cells of the same character as those at the tips of the pegs, displaying an extreme degree of anaplasia. Within many of the lymphatic channels were masses of extremely large, unequal, anaplastic cells. Mitoses were infrequent. A diagnosis of epithelioma of the skin was made.

The patient has remained free from recurrence or metastasis for one year and is still under observation.

ERYTHROBLASTIC ANEMIA OF CHILDHOOD

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Much confusion exists regarding the anemias of infancy that are associated with enlarged spleens. There seem to be no definite criteria for diagnosis, and consequently the treatment is unsatisfactory. Since the tendency to remove the spleen in most of these cases is prevalent, it is urgent that they be classified correctly so that it may be known which are benefited by splenectomy and which are not. Dr. T. B. Cooley and his co-workers [1] have greatly helped in clarifying these anemias of childhood.

Von Jaksch first described what he called "Anemia Pseudo-leukemica Infantum" in 1889. He described an anemia of infants characterized by deficiency of hemoglobin, decrease in the number of red cells, appearance of nucleated red cells in the circulating blood, anisocytosis, poikilocytosis, a large spleen, slight hepatic enlargement and high leukocytosis. He stated that his cases of so-called von Jaksch's anemia showed a tendency to recovery. Since that time many cases of anemia associated with enlarged spleens in infants have been described in the literature and have been called von Jaksch's disease. The cases described have shown so many different clinical symptoms and so many different blood pictures that many authors have said that the term should not be used, as it does not represent a definite disease, and is applied to various diseases of infancy, many of them being secondary anemias and others perhaps true leukemias. This confusion about the disease existed until Cooley, Witwer and Lee [1] reported seven cases of what might have been called von Jaksch's anemia. The cases reported had the following characteristics in common: 1. There was evidence of a congenital cause. 2. The blood picture showed evidence of overstimulation of the marrow, constant leukocytosis, many nucleated red cells in the circulation and absence of increased fragility of the red cells. 3. There were definite changes in the bones. The cranial bones showed thickening. The roentgenograms demonstrated that the cranial bones in the earlier stages exhibited marrow with a mottled, spongy

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From the Pediatric Department of the Southern Baptist Hospital and the Pediatric Department of Tulane University.

1. Cooley, T. B.; Witwer, E. R., and Lee, P.: Anemia in Children, Am. J. Dis. Child. **34**:347 (Sept.) 1927.

appearance and in the later stages with a striking vertical striation. The long bones showed a thin, transparent cortex and a medulla with an abnormal amount of reticulation. The ilia and scapulae showed a marked fanlike striation. 4. There was a peculiar mongoloid expression of the face. 5. There was evidence of hemolysis. For this disease they suggested the name of erythroblastic anemia.

Since Cooley and his co-workers reported their cases, Hitzrot [2] has reported three cases; Whipple, Reeves and Cobb [3] have added two cases; Wolstein and Kreidel [4] have reported nine similar cases, and Baty, Blackfan and Diamond [5] have reported twenty cases. Vogt and Diamond [6] have given a full description of the roentgen appearance of the bones in erythroblastic anemia. All cases reported so far have come from the region of the Mediterranean Sea.

Because of the full descriptions of the clinical and pathologic aspects of this disease that have been given by the writers named, we shall not give them here, but shall simply report our case.

REPORT OF A CASE

History.—An Italian girl born in August, 1925, came to the clinic in the New Orleans Dispensary for Women and Children in August, 1929, complaining of fever and jaundice. The family history was unimportant. She was the youngest of three children; the other two were normal. The mother and father were well. The mother had had no miscarriages and her blood showed a negative Wassermann reaction. The birth of the child was normal and she seemed healthy until she was 3 months old, at which time she had whooping cough. After that time "she did not thrive." When she was 4 months old, the mother first noticed that the abdomen was large. When she was 12 months old she was admitted to a hospital "because there was a lump in her abdomen which was growing larger, and because she was vomiting her food." She remained in the hospital about seven months. While she was there the spleen was removed. From the time of operation, "she has remained fairly well but has had frequent attacks of fever and jaundice."

Examination.—When she came to the clinic, just three years after the operation, she was jaundiced and had a temperature of 102 F. Physical examination showed a fairly well nourished child of average size for her age. The skin and mucous membranes were very yellow. The tonsils were much enlarged and red, and their crypts were filled with a cheesy white substance. The heart and lungs were normal. The abdomen showed a linear scar, but otherwise was normal. The liver was not enlarged.

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2. Hitzrot, J. M.: Ann. Surg. **88**:361 (Sept.) 1928.

3. Whipple, A. O.; Reeves, R. J., and Cobb, C. C.: Ann. Surg. **88**:380 (Sept.) 1928.

4. Wollstein, M., and Kreidel, K. V.: Familial Hemolytic Anemia of Childhood—von Jaksch, Am. J. Dis. Child. **39**:115 (Jan.) 1930.

5. Baty, J. M.; Blackfan, K. D., and Diamond, L. K.: Blood Studies in Infants and Children, Am. J. Dis. Child. **43**:667 (March) 1932.

6. Vogt, E. C., and Diamond, L. K.: Congenital Anemias, Roentgenologically Considered, Am. J. Roentgenol. **23**:625 (June) 1930.

The laboratory data were as follows: total red cells, 2,350,000; hemoglobin (Dare), 46 per cent; hemoglobin (Tallqvist), 50 per cent; nucleated red cells, 174,000, and total white cells, 23,700. The differential count of the nucleated cells showed: neutrophils, 33; lymphocytes, 67; large mononuclears, 14; eosinophils, 6; nucleated red cells, 880, and the total number of cells counted, 1,000. The red blood cells showed normal resistance to salt solution. The stool showed the presence of bile, but examination was negative for ova or parasites. Urinalysis was negative for albumin and sugar and positive for indican, and bile was not present.

Fig. 1.—Roentgenogram of the skull, showing marked thickening of the medullary portion.

Course.—Her throat was painted with silver nitrate and she was given salicylates and sent home with instructions that she be kept in bed as long as she had fever. She returned in a few days with the jaundice lessened, but she still had a muddy complexion. After this time she had several attacks of tonsillitis, and we advised that she be admitted to the Southern Baptist Hospital to have the tonsils removed. The blood count on admission to the Baptist Hospital was practically what it had been when it was made in the dispensary. She was given three transfusions of blood before the removal of the tonsils, but no permanent change occurred in the blood picture. There were 5 per cent reticulocytes in the blood; the icteric index was 40 per cent; the delayed van den Bergh reaction was positive; the calcium content of the blood was 10.5 mg., and the phosphorus was 4 mg.

The tonsils were removed, and she made an uneventful recovery. She gained weight rapidly, and went home three weeks after the operation.

The child has returned to the clinic at the New Orleans Dispensary at varying intervals since discharge from the Baptist Hospital. She has developed and grown normally and has remained fairly well, but she has had several attacks of jaundice and unexplained fever.

Fig. 2.—Roentgenogram of the long bones, showing motheaten appearance.

Roentgenograms of the skull, long bones, hands and pelvis were made by Drs. Samuel and Bowie. We received from them the following report: "Roentgen examination of the long bones, pelvis, hands and skull shows marked peculiarities throughout practically all the bones examined. There is a peculiar motheaten appearance, which is most marked in the bones of the hands and arms. There are numerous transverse lines of increased density. The skull shows marked thickening, especially anteriorly in the lateral view where the thickness amounts to 2.5 cm.

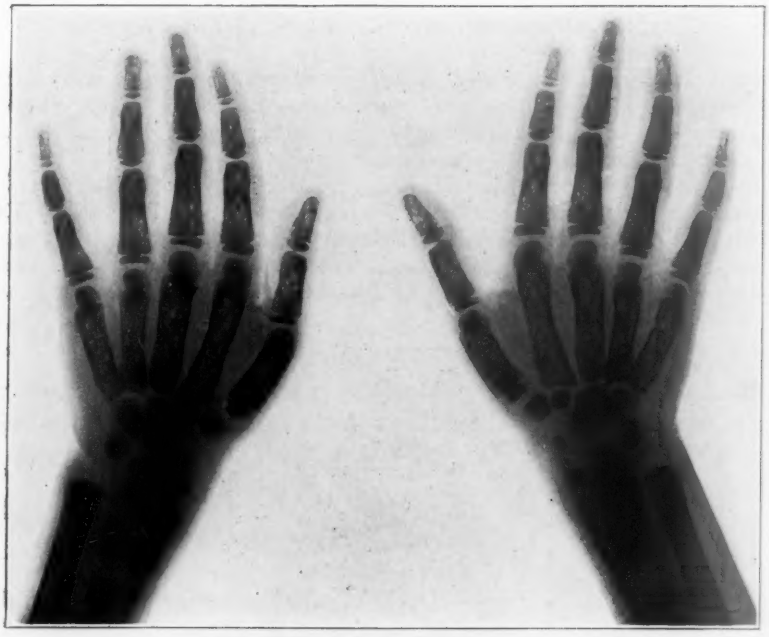

Fig. 3.—Roentgenogram of the hands, showing motheaten appearance.

Fig. 4.—Roentgenogram of the pelvis: note the transverse lines of increased density.

The thickness seems to be entirely confined to the medullary portion of the skull overlying the inner plate, which is not altered in any respect. A peculiar striated appearance is to be seen in the ilia. There is a certain amount of decalcification, but no actual destruction of bone is seen.

These roentgenograms, by some chance, were lost, but we had others made at the Southern Baptist Hospital, which are shown in figures 1, 2, 3 and 4. The photograph of the patient exhibits the thickened malar bones and the enlargement of the skull in the region of the forehead. She had enlarged parietal bosses and a depression along the whole of the longitudinal suture, which do not show in the photograph.

COMMENT

Cooley, Witwer and Lee said of the cases of erythroblastic anemia which they reported that the changes in the bones are the result of the

Fig. 5.—Photograph of the patient, showing the thickened malar bones and the enlargement of the skull in the region of the forehead.

reaction of the marrow to prolonged overstimulation as a consequence of chronic hemolysis beginning before the cortex is too firm to permit the growth of marrow. In earlier stages and in less severe cases, the porous appearance in the roentgenograms seems to represent marrow hyperplasia, while in the terminal stages the pronounced striation indicates the replacement of exhausted marrow by new bone.

The spleen in our patient was removed in September, 1926, and at the time of writing, five years and nine months later, she seems to be growing normally and is fairly well nourished. During the last few months she has shown signs of dyspnea when she runs or plays, and a soft systolic murmur has developed in the heart. The hemoglobin remains about 40 or 50 per cent, and there are about seven times as

many nucleated red cells as there are white cells. The liver has become much enlarged in the last few months, and now reaches 2½ inches (6.3 cm.) below the costal margin in the mammillary line. She has occasional attacks of fever and jaundice, but she rarely stays in bed even when she has the attacks of fever.

It is evident that our patient is suffering from one of the hemolytic anemias. In sickle cell anemia there is a definitely shaped red cell which is not found in the blood of our patient. Hemolytic jaundice does not show an increase in the white cells as the disease in our patient has done, and it shows red cells with a decreased resistance to hypotonic salt solution. Hemolytic jaundice is cured by splenectomy, and the blood does not show a great increase in the nucleated red cells after the operation. Our patient has shown the clinical and pathologic symptoms of the erythroblastic anemia of Cooley.

Progress in Pediatrics

ATELECTASIS OF THE NEW-BORN

A STUDY AND CRITICAL REVIEW

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Atelectasis of the new-born has received scant attention in recent years, despite important advances which have been made in closely related fields. In current textbooks of pathology and of pediatrics, the subject is usually treated briefly, and its presentation is based on traditional conceptions. Certain interesting and highly skilful researches by earlier investigators have been forgotten by later writers. That the term atelectasis of the new-born has been loosely used and its significance misunderstood is shown by the frequency with which atelectasis has been regarded as a complete and satisfactory cause of death, not only in mortality records, but also in autopsy protocols.

Clinical and pathologic observations on more than five hundred premature and full-term babies, as well as experimental studies made in the past few years, have led us to a reconsideration of the problem of atelectasis of the new-born. We shall particularly consider the following points:

1. The histologic differentiation between atelectasis of a lung that has never been expanded and "resorption" atelectasis.
2. The degree of expansion of the lungs with the first breath.
3. The differences between the lungs of premature and of full-term infants.

A review of the literature with special reference to these questions will be made, followed by a report of our own observations. The pathogenesis of atelectasis of the new-born will be treated elsewhere. We shall make no attempt to consider atelectasis of the older child or the various types of collapse of the lung.

TERMINOLOGY

Literally, the word atelectasis means absence of final dilatation of the lungs (a-tel-ectasis) and is used solely in reference to the lung. In new Latin, a slightly altered derivation has been given (atelo = incomplete, ectasis = expansion). Atelectasis refers particularly to the state of expansion of the alveolus, the terminal unit of the respiratory structure of the lung. The word alveolus, or

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alveolar space or sac, will be used in this presentation as the designation for the smallest end-structure of the respiratory system.

According to Bloom,[1] the respiratory bronchioles begin with a diameter of about 0.5 mm. They are relatively short tubes, lined in their first part with ciliated columnar epithelium which contains no goblet cells. A short distance down the bronchiole, the ciliated columnar epithelium gives way to cuboidal or flattened nonciliated epithelium. These bronchioles have walls composed of collagenous connective tissue in which bundles of interlacing smooth muscles and elastic fibers course. There is no cartilage in their walls. A few alveoli bud off from the side of the pulmonary bronchiole opposite that along which the branch of the pulmonary artery runs. These alveoli are the first of the respiratory structures of the lung and are responsible for the term respiratory bronchiole. These bronchioles soon branch and radiate conelike into from two to eleven alveolar ducts which extend for relatively long distances. They are surrounded on all sides by alveoli which have arisen from adjacent ducts.

From the alveolar ducts arise single alveoli and alveolar sacs containing from two to four or more alveoli.

The term alveolar epithelium will be used in this article in the traditional sense as a designation for the lining cells of the alveoli. The fact that in recent years the epithelial origin of the lining cells of the alveoli has been questioned by some and denied by others must be mentioned.

HISTORICAL REVIEW OF ATELECTASIS OF THE NEW-BORN

General Data.—Until 1832 atelectasis of the new-born had been observed and described, particularly by French authors (Valleix, Billard and Grisolle [2]), as congenital pneumonia. The fact that the lungs of the new-born possess nongranulated cut surfaces was presented as the main point of difference between the pneumonias of childhood and those of adult type. In 1832, H. Joerg [3] described this condition as a residue of fetal life and as the result of imperfect respiration, that is, as an incomplete expansion of the lungs with air. In 1841, Hasse [4] pointed out the anatomic differences between atelectasis and certain inflammatory conditions, and substantiated fully the work of Joerg. Three years later, Legendre [5] and Bailly observed the same condition in older children, and declared that atelectasis as found in new-born infants is not a remnant of the fetal state as Joerg and Hasse claimed, but rather a retrogression to that condition. The following year Mendelssohn [6] was the first to apply experimental methods to the production of atelectasis. He showed that the changes after cutting off the vagus were atelectatic. He further endeavored to produce atelectasis of one lung in animals by opening the corresponding pleural cavity. If the animal died soon after the operation, the lung could be inflated, which, however, could not be done if death

1. Bloom, W.: Textbook of Histology, Philadelphia, W. B. Saunders Company, 1930.

2. Cited in von Ziemssen, H.: Cyclopaedia of the Practice of Medicine, New York, William Wood & Company, 1875, vol. 5, p. 322.

3. Joerg, H.: Dissert., Leipzig, 1932; footnote 2.

4. Hasse, K. E.: Specielle pathologische Anatomie, Leipzig, W. Engelmann, 1841; footnote 2.

5. Legendre, F. L. A.: Recherches anatomo-pathologique et cliniques sur quelques maladies de l'enfance, Paris, V. Masson, 1846; footnote 2.

6. Mendelssohn, A.: Der Mechanismus der Respiration und Circulation, Berlin, B. Behrs, 1845.

occurred after a long time. Mendelssohn was the first to state that atelectasis and pneumonia of early childhood were different degrees of development of one and the same process, a belief which has been restated at intervals since that time. He showed that atelectasis gives rise to a condition of stasis in the capillaries which may be followed by exudation, the development of plastic material in the alveoli, and finally pneumonia. Traube [7] (1846) described atelectasis as it occurs in adults. Friedleben [8] (1847) described the clinical symptoms corresponding to the anatomic changes, and pointed out the criteria for the differential diagnosis between atelectasis and pneumonia, which were so often confounded with one another.

In the next ten years a series of papers appeared dealing with the subject of atelectasis (Rees, Donders, West, Cohn, Graily, Hewitt and a number of others [9]). Hewitt [10] used the word apneumatosis as a synonym for pulmonary collapse, and gave credit to Fuchs for the introduction of that term. In 1871, Hertz [11] described atelectasis as a condition of the lungs not due to the filling of the alveoli with fluid or with a coagulable material. This he called congenital atelectasis, or apneumatosis, or *état fœtal de poumon* (Legendre [5]).

As long ago as 1851, Weber [12] stated much that we now believe. He remarked that atelectasis should not be accepted as the cause of death in the new-born. He maintained that atelectasis seldom causes death, that the cause of the atelectasis should be sought in every case, and that it would be found mainly in the central nervous system. He also believed that pneumonia in the first two days of life is frequently confused with atelectasis. His diagnostic points for atelectasis are interesting. He stated them as follows:

"On the surface of atelectatic lungs every little lobule is sharply circumscribed by white lines of connective tissue. These are not found in pneumonia." (Weber believed that lobar pneumonia is the only type of pneumonia found at birth, infection having occurred during fetal life.)

"On cut section the atelectatic lung shows small lobules and almost roughly nodular structure which is not present in pneumonia.

"The atelectatic lung is always firm. The thin anterior borders hang down because of their weight and simultaneous thinness. The pneumonic lung is compact and stands out firmly.

"The atelectatic lung is poor in blood. The pneumonic lung has a great deal of blood. Both pneumonic and atelectatic lungs sink in water."

Weber did not believe that the fact that the lungs do not cover the pericardial sac is of any importance, because pneumonia at the base of the left lung gives the same picture.

The experimental work of Mendelssohn [6] (1845), Traube [7] (1846) and Lichtheim [13] (1879) on the relation of bronchial obstruction to the occurrence of atelectasis of obstructive type must be mentioned here, because these observations, with later refinements, have led to the erroneous conclusion that the same mechanism (obstruction) explains atelectasis of the new-born.

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7. Traube, L.: Beitr. z. exper. Path. u. Physiol. **1**:184, 1846.

8. Friedleben: Arch. f. physiol. Heilk. **6**:408, 1847.

9. Gerhardt, C.: Lehrbuch der Kinderkrankheiten, Tübingen, H. Laupp, 1871, vol. 3, p. 317.

10. Hewitt, G.: Lancet **1**:625 (June 20) 1857.

11. Hertz: Lungs, in von Ziemssen.[2]

12. Weber, F.: Beiträge zur pathologischen Anatomie der Neugeborenen, Kiel, Carl Schröder & Co., 1851, vol. 2, p. 47.

13. Lichtheim: Arch. f. exper. Path. u. Pharmakol. **10**:54, 1879.

Differentiation Between Initial and Resorption Atelectasis.—The differentiation between atelectasis of a lung that has never been expanded (initial atelectasis) and atelectasis of a lung that has been expanded but has subsequently collapsed (resorption atelectasis) has received no special attention in the literature. Although there has been considerable controversy, as will be mentioned later, as to the relative importance of these two types in the new-born infant, no definite pathologic criteria for this differentiation have been given.

Considerable work, mostly based on histologic study, has been carried on, however, in an attempt to analyze the changes that take place in the pulmonary parenchymal cells during fetal life and just before birth, and to explain the transition from the cuboidal cells of the fetal lung to the flat alveolar lining cells of the fully expanded lung of the normal infant.

Fauré-Fremiet [14] showed that in the development of the epithelium of the lung of the sheep there occurs a change just before birth. While the connective tissue of the parenchyma of the lung continues to increase, the epithelium apparently does not increase sufficiently to cover the alveolar walls. This discrepancy in growth must of necessity cause a dehiscence of the epithelial covering of the alveoli. In 1920 Ogawa [15] studied the embryogenesis of the respiratory epithelium, and concluded that during fetal life there is a gradual partial flattening of the originally cuboidal epithelium, so that near term the epithelium consists of two elements: cuboidal cells arranged in groups and flatter elements which lie between these cuboidal cells. The flat elements lose their nuclei near term through an increase in the processes of pyknosis, karyorrhexis and chromatolysis. In this way non-nucleated plates are formed.

An interesting study of the lungs of rats was made by Stewart [16] in 1923. He examined the histologic changes which took place from day to day in the lungs of the rat fetus. He found that in the 17 day old rat fetus the parenchyma consists of columnar epithelium with oval nuclei and densely granular cytoplasm. During the eighteenth day, a marked alteration becomes apparent, and is accentuated on the nineteenth day. The pulmonary epithelium becomes swollen and, on successive days, more hydropic. With this hydropic transformation and possibly because of it, the cytoplasm of the epithelial cells undergoes a sort of fatty metamorphosis. Microscopically, the cytoplasm becomes practically structureless. The fat content of the connective tissue becomes increased, and through a process of fatty degeneration the connective tissue in part disappears.

Stewart expressed the belief that these processes prepare the lungs for postnatal expansion. By degeneration of the connective tissue, space is provided for expansion of the alveoli. The cytoplasm of the cuboidal epithelial cell is rendered considerably more plastic through the imbibition of fluid. It is less firm and rigid at this period and is more capable of deformation. The epithelial cell itself, he held, is changed from a cuboidal to a flat form either by pressure brought about by gasping movements in utero or by the first postnatal inspiration. In the process of expansion either the various epithelial cells must be sufficiently plastic to line the alveoli completely, or else for a time some portion of the alveolar wall must remain naked of epithelium.

The hydropic character of the cell may be due to its slow, absorptive process, continued over a considerable period. This was suggested by the work of

14. Fauré-Fremiet, E.: Compt. rend. Soc. de biol. **83**:11, 1920.
15. Ogawa, C.: Am. J. Anat. **27**:333, 1920.
16. Stewart, F. W.: Anat. Rec. **25**:181, 1923.

Wislocki,[17] who concluded that amniotic fluid reached the lung of the fetus during intra-uterine life, and that small amounts of amniotic fluid are absorbed through the lower respiratory tract. Although Stewart was unable to prove that fluid was imbibed by the epithelial cells, in repetitions of the experiments described by Wislocki, he concluded that it was possible for such imbibition to occur and thus explain the hydropic appearance of the epithelial cells in the latter period of fetal life.

Wislocki remarked that every one who has worked on pregnant animals is aware of movements resembling respiration during the latter part of pregnancy. This recalls the observations of Ahlfeld[18] made in 1881 and confirmed by Reifferscheidt[19] in 1911, on the occurrence of certain rhythmic movements in the fetus at a rate of from 38 to 76 per minute. They are best felt near term in the region of the umbilicus of the mother and are interpreted as being caused by movements of the respiratory muscles.

We should like to suggest that the anatomic changes in the pulmonary epithelium described by Stewart might well be correlated with the physiologic observations of Ahlfeld and Reifferscheidt. It is conceivable that the changes in the plasticity of the pulmonary epithelium are merely an anatomic expression of widespread activity of the lung in preparation for extra-uterine existence.

Seemann[20] (1932) concluded from the work of Ogawa and of Stewart and from his own similar observations that the development of the pulmonary epithelium occurs through flattening and dehiscence of the originally continuous cuboidal epithelium, and that this occurs in the last period of fetal life and is completed by the time birth takes place. Through expansion of the pulmonary tissue with the first breath, this flattening process merely becomes more marked.

Degree of Expansion of the Lungs with the First Breath.—The belief that the lungs expand fully with the first breath is still held. For more than fifty years this question has sorely vexed a number of workers, particularly in Germany. The conception that with the first breath the alveoli become greatly distended and the cuboidal epithelial cells lining the alveolar spaces immediately flattened is time-honored; it is still given in a number of current textbooks, and is maintained by some present-day workers, notably Ylppö[21] and Loeschke.[22] The belief

17. Wislocki (Contrib. Embryol. **11**:47, 1920) injected a 1 per cent solution of potassium ferrocyanide and iron ammonium citrate into the amniotic sac after withdrawing an equal amount of amniotic fluid. After thirty minutes, the fetus was immersed in acid formaldehyde, and prussian blue was precipitated in the lungs. Wislocki concluded that the failure to find lanugo hairs and other material in the respiratory passages does not militate against the conclusion that some amniotic fluid is absorbed through the lower respiratory tract during fetal life, because the epiglottis might readily prevent gross material from entering the lungs.

18. Ahlfeld, F.: Monatschr. f. Geburtsh. u. Gynäk. **21**:143, 1905.

19. Reifferscheidt, K.: Deutsche med. Wchnschr. **19**:877, 1911.

20. Seemann, Georg: Histobiologie der Lungenalveole, Jena, Gustav Fischer, 1931.

21. Ylppö, A., in Langstein, Leo: Beiträge zur physiologischen Pathologie und sozialischen Hygiene des Kindesalters, Berlin, Julius Springer, 1919.

22. Loeschke, H., in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1928, vol. 3, p. 599.

is attractive because of its simplicity, but that changes much more subtle than the immediate flattening of lining cells must be considered has been shown by recent studies.

Several approaches to this question have been utilized by investigators: observations on the animal fetus, cytologic studies of the lungs of animals, measurements of the respiratory exchange in the new-born and histologic studies of the lungs of new-born infants.

In Germany, the view that the lungs expand fully at birth was championed by Ungar,[23] who carried on a long controversy with Dohrn[24] and later with Peiser.[25] Ungar believed that atelectasis of the lungs of infants who had lived a few days was due to the absorption of air from previously expanded alveoli, a fact of great medicolegal importance. From experiments on the fetuses of rabbits, dogs and cats, Ungar found support for his theories. He removed the young from the uterus just before term, after tying off the neck of the fetus. He then permitted them to breathe one or two times and again tied off the trachea. The lungs were then removed and were found to be completely expanded. It should be noted, however, that no microscopic studies were made.

The investigations of Dohrn[24] and his pupil Eckerleis were concerned with the measurements of the amount of respiratory exchange in the first few days of life. They showed that the capacity of the lungs roughly doubled during the first six hours after birth, and increased progressively for several days. Dohrn concluded from these observations that not all parts of the lung were expanded at one time, and that expansion of the lungs is a gradual process. Ungar and his pupil Buechner utilized Dohrn's method and came to a similar conclusion; namely, that the respiratory exchange directly after birth and during the first day of life is small, and that it increases markedly by the second day. However, Ungar maintained that these findings can be interpreted as proof that all parts of the lungs are expanded immediately after birth so far as the number of expanded alveoli is concerned, but that the individual alveoli are not so fully expanded as on the second day after birth. More recently Ylppö[21] and Loeschke[22] concluded that all atelectasis of the new-born is of a secondary resorption type. They expressed the belief that the lungs of a new-born infant are fully expanded by the first breath, but that owing to faulty or insufficient respiration from various causes which lead to death, the air is resorbed and secondary atelectasis occurs.

Addison and How[26] (1913) showed by measurements on cross-ruled millimeter paper that the pulmonary tissue in sections of the fetal lungs of the dog constitutes 70 per cent of the entire area; in sections of the lungs of dogs which had breathed for one hour, from 40 to 60 per cent, and in sections of the lungs of dogs which had breathed for two days, from 20 to 30 per cent. These measurements, they believed, were proof of the gradual expansion of the lungs after birth.

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23. Ungar, E.: Jahrb. f. Kinderh. **69**:505, 1909; Vrtljschr. f. gerichtl. Med. **13**:63 and 86, 1897.

24. Dohrn, W.: Verhandl. d. deutsch. Gesellsch. f. Gynäk. **3**:102, 1890.

25. Peiser, J.: Jahrb. f. Kinderh. **67**:589, 1908.

26. Addison, W. H. F., and How, H. W.: Am. J. Anat. **15**:199, 1913.

Another approach to the subject was made by microscopic examination of the lungs. Elenz [27] (1864), Colberg [28] (1867), Laguesse [29] (1886) and Stieda [30] (1878) maintained that the process of flattening of the respiratory epithelium is gradual, occurring during fetal life, but that the postnatal expansion of the lungs is of the greatest importance in converting the cuboidal cells into non-nucleated plates. Küttner,[31] on the basis of experimental work, stated that the epithelium remains cuboidal until flattened by the first respiratory movements. His method consisted in first silvering the epithelium and subsequently injecting gelatin. On examination, he noted that the portion of the lung into which no gelatin was injected showed a cuboidal epithelium, whereas in the region into which an injection was made the epithelium was flattened. Jalan de la Croix [32] agreed with the observations of Küttner, and, as Stewart [16] has phrased it, terminated his paper with the expression of a devout hope that he had once and for all settled the question. Kölliker [33] (1884) believed that after birth, because of pressure by breathing, the epithelial cells were changed to non-nucleated plates, while the epithelial cells between the capillary loops were protected from the pressure and therefore were unable to maintain a more or less cuboidal form.

Difference Between Atelectasis of the Full-Term and That of the Premature Infant.—Although atelectasis in both full-term and premature infants has been the subject of considerable investigation, we have found no studies reported in which any differentiation from a pathologic point of view has been made between the types of atelectasis found in the lungs of the premature baby and in those of the full-term infant.

Ylppö [21] recently studied the lungs of premature infants. He described microscopically the lungs of eleven infants, one of whom was a full-term, new-born infant and one a premature infant weighing 2,300 Gm.; the remainder varied in weight between 990 and 1,500 Gm., and had lived from thirty minutes to sixteen days. Ylppö came to the conclusion that atelectasis of the premature infant is similar to that of the full-term infant. He did not, however, explain in his own illustrations the absence of lumens in large areas of pulmonary tissue, representing masses of alveolar lining cells.

A suggestion that there may be an essential difference between the lungs of premature and of full-term infants can be found in an interesting observation made by Addison and How.[26] They studied the lungs of a kitten born one week before the remainder of the litter. The kitten had the appearance of a healthy normal animal and crawled about and cried vigorously when disturbed. It lived only about twelve hours. On section, the bronchi were much distended, but only a few of the respiratory spaces were inflated. Those that were distended, however, were overexpanded. The remainder of the lung was denser than an ordinary fetal lung. Addison and How were able to compare the lungs of this kitten with the lungs of a full-term kitten of the same litter born one week later which had also lived twelve hours. The lungs of the full-term kitten showed much more expansion than the lungs of the prematurely born kitten. The investigators concluded that respirations in the prematurely born kitten had begun before the lungs were "sufficiently developed to assume their normal function."

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27. Elenz, E.: Würzb. naturw. Ztschr. **5**:66, 1864.
28. Colberg: Deutsches Arch. f. klin. Med. **2**:455, 1866.
29. Laguesse, E.: J. de l'anat. et physiol. **22**:211, 1883.
30. Stieda: Ztschr. f. wissensch. Zool. **30**:706, 1878.
31. Küttner: Virchows Arch. f. path. Anat. **66**:12, 1876.
32. de la Croix, Jalan: Arch. f. mikr. Anat. **22**:93, 1883.
33. Kölliker: Sitzungsb. d. phys.-med. Gesellsch. zu Würzburg **16**:1, 1880.

PRESENT OBSERVATIONS

Gross and Microscopic Appearances of Atelectasis of the New-Born.—The lungs of an infant who has never breathed are uniform in color and consistency and lie in the floor of the pleural cavity in a collapsed state, so that none of the pulmonary surfaces or edges touch the pericardial sac. They are deep purplish red and have smooth, nongranular surfaces covered by thin, transparent pleura through which the pulmonary tissue can be clearly seen. The consistency is similar to that of the thymus and is frequently compared to raw meat. No crepitus can be elicited on palpation, and the lobules of the lungs cannot be identified through the pleura. When breathing has taken place, the areas which have been expanded stand out prominently beneath the pleura, and the fibrous septums which serve as delimiting markings of the lobules are easily recognized. The expanded areas rise above the darker, unexpanded portions of the lungs.[34] In infants who have breathed for a few hours, the anterior surfaces are pale pinkish blue, and the lobulations stand out clearly. The pleura is no longer wrinkled, but is pulled taut over the expanded areas. The anterior portions are the first to expand, and the most prominent portion is the lappet of the left lung, which extends medially and partially covers the pericardial sac.

On section through an unexpanded lung, the surfaces are firm, airless and deep purplish red. Blood can be forced from the vessels in small amounts, but no air can be expressed from the parenchyma of the lungs on pressure. Crepitus is absent. The surfaces are meaty, and faint connective tissue markings can be found on careful examination. If expansion has not taken place, the whole lung will sink when placed in water. However, if partial expansion has occurred, the small purplish-red, noncrepitant areas of pulmonary tissue, when cut from the rest of the lung, will sink when placed in water.

We have found that gross examination of the lungs is insufficient to determine the extent of expansion accurately. The fact that on micro-

34. Peiser [25] maintained that the apparent appearance of sunken areas characteristic of atelectasis is due to an artefact, and that when the lungs are fixed by special methods, such areas cannot be found. He used the method of Gregor. Before the thorax is opened, a diluted solution of formaldehyde, U. S. P., (1:3) is injected into the inferior vena cava under light pressure until foamy fluid wells out of the mouth and the nose. Autopsy is carried out the following day. Peiser reported his findings in the lungs of nine infants treated in this manner. Eight were either new-born or had lived a short time after birth. The ninth was a 9 months old baby who had died of pneumonia and empyema. Peiser could demonstrate no difference in the level of the atelectatic portions as compared with the portions which had been expanded. His method is open to criticism, because if sufficient pressure is used to force foamy fluid out of the mouth and the nose, it is also sufficient to cause expansion of the atelectatic portions of the lung.

scopic section an apparently fully expanded lung may contain large amounts of noninflated pulmonary tissue represented by scattered nests of unexpanded alveoli must be kept in mind.

On microscopic examination of pulmonary tissues in which the state of expansion of the air spaces is in question, it must be realized that the degree of dilatation of the lung is changed when the lung is removed from the thoracic cage. It no longer is subject to the slight negative pressure of the thorax which maintains some distention even in the dead body, but collapses to a considerable extent after removal. It is to be noted, however, that for comparative purposes this factor may not be of great importance, since all lungs are necessarily sectioned under a similar condition. The degree of expansion of an alveolus in a section of pulmonary tissue depends primarily on the state of elasticity of the lung—an elastic state that apparently resists both complete collapse and distention beyond a certain point.

Experience makes us believe, however, that the passive state of expansion of excised pulmonary tissue is consistently influenced by conditions existing before death and evidently reflects in a fairly dependable manner a state of emphysema or collapse maintained even for a short time before death.

In order to determine the effect of the preparation of tissue on the size and appearance of air spaces on microscopic examination, a series of sections of lungs was made by a variety of methods. Several fixatives were employed, and the tissue was fixed with the lungs in toto as well as in the form of small, excised portions. Sections embedded in paraffin and pyroxylin (celloidin) and frozen sections were used in preparing the slides, suitable blocks being chosen for comparison. So far as the state of expansion of the air passages is concerned, no noteworthy differences were found which might lead to a false histologic picture with any of the methods except with the frozen section technic. In sections prepared according to this method, the existing spaces are increased in size, and a greater degree of expansion of the lung is shown than is present in sections made by the other methods.

When prepared according to the various technics, microscopic sections of the lungs of the new-born baby who has never breathed show that the terminal bronchioles and the alveolar ducts possess definite though very small lumens. The connective tissue of the lung appears very prominent in contrast to the unexpanded alveoli. The alveoli may have tiny, slitlike openings, or, in many cases, the spaces may not appear definite, owing to the encroachment of the large cuboidal lining cells.

Histologic Differentiation Between Initial Atelectasis and Resorption Atelectasis.—The work of Küttner, Ogawa, Stewart, Seemann and a number of other investigators points to the facts that the epithelium of

the lung is prepared for expansion before birth, and that certain important changes in the epithelial cells have already occurred before the first breath takes place. It is impossible, of course, to carry out studies on infants comparable to those made by Stewart on the rat, and doubt may well be expressed in regard to the exactness with which the observations on rats may be applied to infants' lungs. The duration of pregnancy in the human being is altered by so many factors not met with in the rat that it is conceivable that the alterations in the pulmonary epithelium described by Stewart may be either decreased by a slightly premature delivery or accentuated by a prolonged labor. In either of these possibilities or in any of the numerous possible intermediate gradations, a study of the lungs of human beings at birth or shortly thereafter could not be expected to yield so simple or so uniform a picture as that seen in experimental animals. And such, indeed, was the case in our study of the lungs of new-born babies. We have frequently seen the so-called hydropic degeneration of the alveolar lining cells in the lungs of new-born babies, but we find it difficult to evaluate the significance of such changes, because of the frequency of the formation of artefacts of this nature.

As we have mentioned, Ylppö and Loeschke believe that the new-born infant fully expanded his lungs with his first breath, and that atelectasis of the new-born was due to a secondary resorption of air because of inadequate or enfeebled respirations. From our observations we have not been able to agree with these investigators. We have paid particular attention to the possibility of accurate histologic differentiation between resorption atelectasis (in a lung which has previously been expanded) and initial atelectasis (in a lung which has never been expanded). We have been able to show that the high cuboidal cells lining the alveoli of the lungs of the full-term fetus become flattened mechanically by distention of the alveolar spaces.

In order to show this experimentally, we carried out the following procedure. Lungs of stillborn babies were removed and suspended in an improvised Drinker respirator, the trachea being connected to the outside by suitable tubing. One main bronchus was clamped off at the bifurcation of the trachea to allow one lung to serve as a control, and the other lung was allowed to become gradually expanded by the action of the respirator. Histologic study demonstrated clearly the flattening of the cuboidal alveolar lining cells of the expanded lung as contrasted with those of the control lung by the simple mechanical action of the respirator on the dead tissues.[35] Microscopic study of the lungs

35. This observation is illustrated also by the experiments of Küttner.[31] The pressure of the gelatin injected into the lungs caused flattening of the epithelium, while in the regions into which no injection was made, the epithelium remained cuboidal in shape.

of infants who had breathed well for a number of days and who presented areas of resorption atelectasis at autopsy confirmed these observations. The cells lining the collapsed alveoli were flattened, irregular in position and unevenly spaced along slightly tortuous alveolar walls, as contrasted with the regular, even spacing of cuboidal epithelial cells lining an alveolus which had never been expanded (fig. 1).

We believe, therefore, that it is possible to differentiate histologically by observations on the shape and position of the alveolar lining cells between an alveolus that has never been expanded and one which has been expanded and subsequently collapsed after the resorption of air.

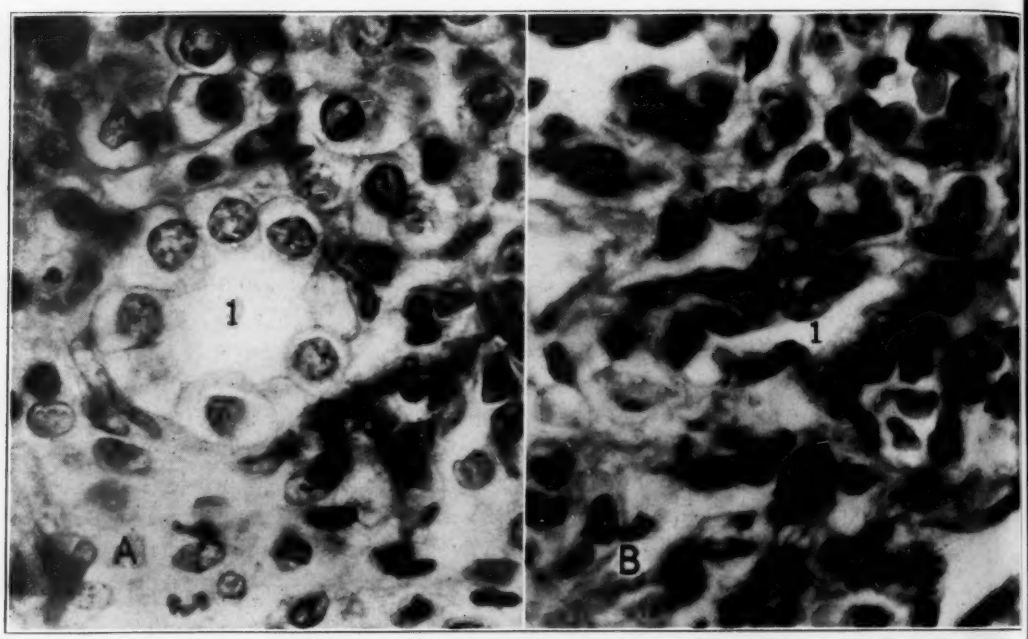

Fig. 1.—Photomicrographs of lungs for the comparison of initial and resorption atelectasis. *A* represents the lung of a new-born infant, showing an alveolus (indicated by *1*) which has never been expanded. Note the high cuboidal cells with regular spacing lining the alveolar wall. There is no evidence of flattening. *B* represents the lung of an infant who had lived eight days. In the alveolus indicated by *1*, note the irregular position, uneven spacing and flattening of the lining cells. Hematoxylin and eosin stain; reduced from a magnification of × 445.

A detailed report of this problem and its medicolegal implications will be given elsewhere.

Degree of Expansion of the New-Born Infant's Lungs with the First Breath.—It was concluded by Ungar, Ylppö and others that the lungs are fully expanded with the first breath. We have obtained con-

siderable evidence against this theory from postmortem studies on new-born infants. On microscopic examination, we have frequently found numbers of small unexpanded alveoli with lumens represented only by small slits, that is, areas of atelectasis in the lungs of full-term infants who have lived for from a number of hours to several days. These infants had breathed regularly and well much of the time, and had died from extrapulmonary causes. The alveoli were lined by large cuboidal cells which apparently had never been flattened. These observations show that the antenatal process preparatory to the flattening of the lining cells which was described by Stewart and others in the rat does not hold for all the cells of the lung of the infant. That the alveoli in these unexpanded areas never had been expanded is demonstrated by the absence of flattening in these cells. If the prenatal changes in the plasticity of the epithelial cells as described by Stewart and others in the rat are to be accepted for the lung of the human being, it is impossible to believe that a cell once flattened to the shape usually seen in the completely expanded lungs of an infant can return to a cuboidal form.

From our observations we must conclude that expansion of the lung is a gradual process; that in the full-term infant who breathes well and suffers from no obvious interference with respiration (death being due to such nonrespiratory causes as atresia of the bowel) from two to four days at least are normally required for complete expansion of all portions of both lungs, microscopically as well as grossly, and that a period up to six weeks or longer may be required to inflate fully the lungs of a premature infant.

We have noted that expansion takes place first in the anterior portions of the lungs, particularly in the lappet of the upper lobe of the left lung, and that expansion later extends to the posterior portions of both lungs.

Since a variable period of time is required for full expansion of the lung, it follows that a certain amount of unexpanded pulmonary tissue may be present under normal conditions during the first few days of life. The finding of these areas of atelectasis can then assume no importance in explanation of symptoms or of the mechanism of death, and certainly cannot be accepted in itself as a cause of death of the new-born. From the evidence cited from the literature and from our own observations, it would appear justifiable to speak of a normal or physiologic amount of atelectasis during the first few days of life.

The Lungs of the New-Born Premature Infant.—The differences between the lungs of a premature infant and those of a full-term infant deserve special study. The type of atelectasis found in the premature

infant has been assumed to be the same as that found in the full-term infant.

Although Addison and How [25] did not definitely so state, their findings suggest that some of the atelectasis of the prematurely born kitten is different from that of the full-term animal. Our findings have led us to believe that there is a distinct type of atelectasis found in the lungs of premature infants.

The differences between the lungs of premature and of full-term infants are best explained by recalling that the premature infant is to be regarded anatomically as a fetus born at the sixth, seventh, eighth or ninth month of intra-uterine existence. From a study of the gross and microscopic structure of the lungs of premature infants we were impressed with the fact that a degree of immaturity comparable to the immaturity found in other organs of the body, such as the kidney, is also present in the lungs. We are then dealing with organs which have not reached their full development, and because of the degree of immaturity, certain anatomic differences are found.

From a study of the structure of the lungs of premature infants, we have been able to recognize a type of unexpansion which should be distinguished from the usual types of atelectasis found in the new-born. This type of unexpansion is constantly present in the lungs of premature infants and is proportional in degree to the stage of prematurity of the infant. A brief review [1] of the development of the alveoli will serve to illustrate these differences.

The primitive bronchi are first lined with low cylindric or cuboidal epithelium. They branch dichotomously and are capped by end-buds or end-knobs called pneumoneres. These end-knobs are lined by several layers of cylindric epithelium which differentiate them from primitive bronchi. After the ten week stage, the epithelium of the end-knobs becomes a single layer. The end-knobs continue to branch perpendicularly to the axis of their ducts. In the three to four month stage the pneumoneres, which until then had been dividing dichotomously with regularity, begin to branch irregularly. In the eighteen to twenty week stage, the end-knobs or pneumoneres divide quite irregularly. At six to seven months in a 35 cm. fetus, that is, at a time in development when a great many premature infants are born, the small bronchi are lined in part with ciliated epithelium which flattens toward the peripheral ends of the bronchi. These bronchi branch and end in the terminal duct capped with the end-knobs or pneumoneres. According to most authors, the young pneumoneres finally become alveoli. We were able to follow these sequences in a small series of sections of lungs from embryos and fetuses in various stages of development.

We have made the following observations in our study of the lungs of premature infants: In any state of early prematurity and to an extent roughly proportional to the degree of immaturity, developing pulmonary tissue with irregular division of the end-knobs will be found on microscopic section. These dividing and forming pneumoneres are

indicative of an incompletely developed lung and form masses of cells not capable of expansion, regardless of the amount of pressure used in attempts to inflate them. It may be emphasized that mature, fully developed alveoli are also present in other portions of the lungs of premature babies, and that the fully formed alveoli may remain in the ordinarily recognized state of atelectasis caused by any of the changes which bring about atelectasis in the full-term infant.

On gross examination, the lungs of new-born, premature infants, except for their smaller size, resemble the lungs of new-born, full-term

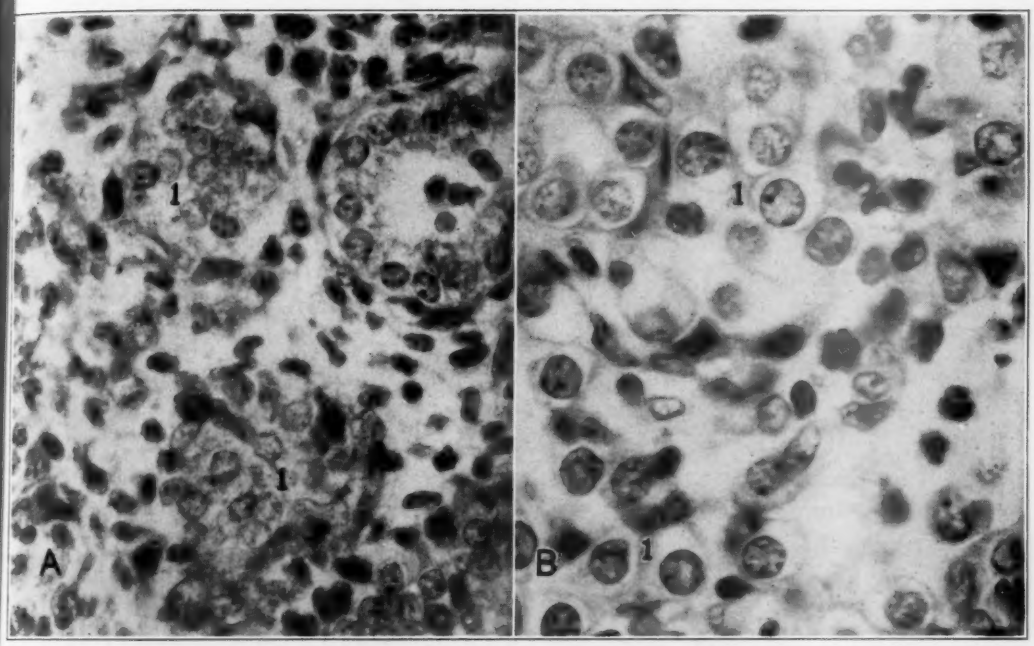

Fig. 2.—*A* represents the lung of a fetus of three and one-half months' gestation. Note the masses of epithelial cells (*1*) without alveolus formation. *B* represents the lung of a premature infant, aged 2 days, weighing 2 pounds (907.18 Gm.). Note the similar masses (*1*) of epithelial cells without alveolus formation. Hematoxylin and eosin stain; reduced from a magnification of × 895.

infants. On microscopic examination, considerable differences are apparent. Between the air-containing spaces are very thick, cellular, alveolar walls. On careful study, it will be seen that many of the air-containing spaces are not alveolar spaces, but dilated respiratory bronchioles and alveolar ducts. In the lungs of very small premature infants true alveolar spaces may be rare. Under higher magnification, many

unexpanded areas of the lungs and much of the apparently thick alveolar walls are found to be composed of large numbers of cells identical in form, size and appearance with those found lining fully formed alveoli in other portions of the lungs and similar to the cells lining the unexpanded alveoli in the full-term infant. These cells are often found arranged in loosely gathered clusters surrounded by mesenchymal cells. Such collections of cells can be traced in serial sections to lumen-containing structures, representative of terminal portions of alveolar ducts, and are identical with cell clusters in the lungs at the third or fourth month of gestation. Alveoli which are fully formed but which have not been expanded, as has been described before, have small lumens surrounded by high cuboidal cells which possess large, round, vesicular nuclei. The free borders of these cells project into the thin slit representing the potential alveolar space, giving such a space a corrugated outline. The masses of alveolar cells which are not sufficiently developed for expansion, on the other hand, are recognized by the massing or clustering of cells identical in morphology with those just described lining fully developed alveoli but without evidence of a definite lumen or true alveolus formation. Depending on the stage of prematurity of the infant, such areas of unexpandable pulmonary tissue may be found for as long as six weeks after birth.

In order to demonstrate the differences between the lungs of premature and of full-term infants by another method, we artificially inflated a series of lungs. If atelectatic lungs of premature and of full-term babies are inflated by pressure or by a modified Drinker respirator, a comparison of the results of the inflation strikingly illustrates the incomplete development of the premature infant's lung. If one lung is clamped off to act as a control, there will appear a marked difference between the expanded and the control lung of the full-term infant. The expanded side may show little or no atelectasis in comparison with the solid structure of the control lung. Very much less effect is seen in the case of the very immature lung. On the expanded side many of the terminal bronchioles and alveolar ducts are distended, but large clusters of incompletely developed and unexpandable alveoli preserve an appearance similar to the control lung.

The significance of these areas of incomplete development can be summarized as follows: In infants born in the fifth or sixth month of fetal life, the presence of large areas of unexpandable pulmonary tissue may make continued life impossible because of the lack of sufficient respiratory epithelium. Bremer [36] has stated that the human fetus is

36. Bremer, J. L., in Lewis, F. T., and Bremer, J. L.: A Textbook of Histology, Philadelphia, P. Blakiston's Son & Co., 1927.

not viable if born before the clusters of end-pieces capable of forming respiratory epithelium are produced. In infants who are born later in intra-uterine life, when sufficient respiratory epithelium has developed to maintain life, large areas of incompletely formed pulmonary tissue may still be demonstrated and may form areas of unexpandable lung explicable entirely on the basis of immaturity, although there may also be present in such lungs numbers of fully developed alveoli which

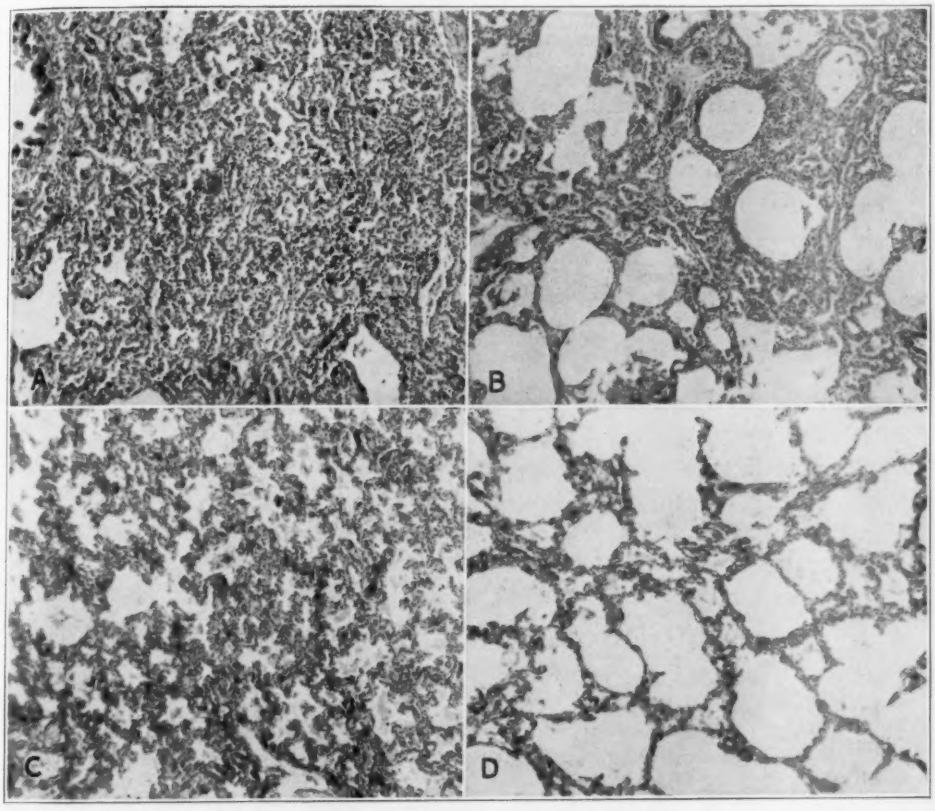

Fig. 3.—Photomicrographs for comparison of the lung of the premature and of the full-term infant when artificially expanded by the action of a Drinker respirator after death. One lung was used as a control (not expanded) in each case. *A* and *B* represent sections of lungs of a premature infant, aged 2 days, weighing 2 pounds (907.18 Gm.). *B* represents the expanded lung. Note that the distention involves mainly the bronchioles and alveolar ducts. The alveoli have not been affected. *C* and *D* represent sections from the lung of a full-term infant, aged 2 days. *D* represents the expanded lung. Note the uniformity of distention of the alveoli, with the greater amount of distention. All pressures were approximately the same. Hematoxylin and eosin stain; reduced from a magnification of × 104.

have not been expanded, constituting atelectasis similar to that found in any new-born baby.

The question of a suitable designation for the areas of incompletely formed pulmonary tissue causes some difficulty. To use the term atelectasis is illogical, for such areas are anatomically unexpandable, and one might as justly speak of an atelectatic liver. The descriptive phrase of Legendre,[5] *état foetal de poumon,* and other similar terms, such as fetal lung and fetal state, are not without criticism, since the designation fetal lung may just as well apply to the lung as found immediately before birth in a full-term infant when development is complete. Prof. W. G. Aurelio (Boston University, Department of Greek) suggested the word *anectatos* to denote the lack of capability of expansion, as contrasted to simple atelectasis. It is perhaps wiser not to attempt the launching of a new word. We suggest that simple recognition of such areas as immature pulmonary parenchyma incapable of expansion because of incomplete development and a sharp differentiation of such areas from unexpanded, fully formed alveoli, indicative of true atelectasis, are the best disposition of this question.

CONCLUSIONS

It has been shown that since the lungs of the normal full-term infant expand gradually over a period of a few days, a variable amount of initial atelectasis will be present normally in all infants during the first few days of life; this may properly be considered physiologic atelectasis of the new-born. The normal existence of a variable amount of atelectasis should be recognized, and its presence at postmortem examination should not be accepted as an adequate cause of death. Because of various factors interfering with the respiration of the new-born, the atelectasis may persist to a pathologic extent. The finding of large areas of this form of atelectasis is of definite importance as one factor leading to death, although, as is shown elsewhere, a cause for the atelectasis must be demonstrated in every case.

Another type has been called resorption atelectasis. This was originally mentioned by Lichtheim and by Ungar, and more recently stressed by Ylppö and Loeschke. This type is found in infants who may have breathed so well for a varying period (at least several days) that the lungs have been well expanded. After some factor has interfered with respiration, the air may be slowly absorbed from many alveoli, with resultant resorption atelectasis. We have shown that if the alveolar spaces have been fully expanded and the lining epithelium flattened, such areas of resorption atelectasis can be differentiated microscopically from the areas of fully developed alveoli which have never been expanded—initial atelectasis—by the position and shape of the

lining cells. The cells lining the alveoli in the areas of resorption atelectasis will not return to their former cuboidal form. The chief importance of recognition of this type of atelectasis lies in the implication that expansion has once taken place, and that subsequently some interference with respiration has occurred.

Any of the types of atelectasis described may be found in premature as well as in full-term infants. However, in addition to these types of atelectasis, there may be present in the lungs of premature infants solid areas of parenchyma superficially resembling atelectasis but explained by incomplete development or immaturity of those areas. This finding does not represent true atelectasis.

SUMMARY

1. The literature concerning the nature of atelectasis of the newborn has been reviewed.

2. The histologic differences between a lung that has never been expanded and one which has been expanded and subsequently collapsed, with resorption of air, have been described.

3. It has been pointed out that the normal expansion of the lung is not completed at the first breath, but that a certain degree of initial atelectasis is physiologic for probably several days after birth.

4. The existence in the lungs of premature infants of areas of incompletely formed pulmonary tissue has been described. These areas do not represent true atelectasis.

PATHOGENESIS OF ATELECTASIS OF THE NEW-BORN

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We have considered elsewhere [1] the differentiation between initial atelectasis and resorption atelectasis, the degree of expansion of the lungs with the first breath, and the presence in premature babies of unexpandable pulmonary tissue, consisting of incompletely developed parenchyma.

The pathogenesis of the ordinarily recognized type of atelectasis in new-born and, particularly, premature infants forms the subject of this study.

The diagnosis of this condition as a complete and satisfactory cause of death, especially in premature infants, is widely accepted. It is obvious that when large areas of atelectasis are found in the lungs of a new-born infant who has died after exhibiting such evidences of imperfect respiratory function as constant or intermittent cyanosis, there must be a relation between the atelectasis and the anoxemia. The atelectasis may be accepted as the immediate cause of the anoxemia. It has seemed to us, however, that so long as the lung is anatomically perfectly developed, it is not logical to accept the existence of atelectasis as a satisfactory explanation of death; that, on the contrary, the atelectasis should be considered secondary to more fundamental causes and its pathogenesis more thoroughly considered.

With the conception that atelectasis in the perfectly developed lung must be secondary, we believe that the factors preventing the initial normal expansion of the new-born baby's lung may be outlined as follows:

1. Cohesion of the moist surfaces of the air passages in collapsed and airless lungs. This "stickiness" of the collapsed airways offers considerable resistance to the entrance of air, and a relatively great

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From the Department of Pediatrics and the Department of Pathology of the Harvard Medical School and of the Infants' and Children's Hospital.

1. Farber, Sidney, and Wilson, James L.: Atelectasis of the New-Born, Am. J. Dis. Child., this issue p. 572.

force is required to overcome it and to separate the bronchiolar and alveolar walls during the initial expansion. The first breath of every new-born baby may thus be its most difficult one, and especially vigorous inspiratory efforts must be maintained for a variable period after birth until the normal atelectasis is finally overcome. This initial resistance of the atelectatic lungs to expansion is always present and contributes to the maintenance of atelectasis to a pathologic extent when it is combined with any of the following factors.

2. An imperfectly developed or an injured respiratory center which does not respond to the normal stimulus and fails to bring about repeated and sufficiently vigorous inspiratory efforts.

3. A poorly developed thorax, especially seen in premature infants when the bony framework of the thorax and the contraction of the intercostal muscles do not furnish an effective *vis a tergo* for the efficient action of the diaphragm.

4. Bronchial obstruction due to aspiration of the contents of the amniotic sac, mucus or blood.

We shall consider these separate factors in greater detail.

COHESION OF THE BRONCHIOLAR AND ALVEOLAR WALLS

If one watches the breathing of infants with extensive atelectasis, one may note certain striking and suggestive features. Although the respiratory movements may be irregular and interrupted by periods of apnea, especially in small premature infants, much of the time the baby may exhibit vigorous respiratory efforts, and at these periods the breathing may strikingly simulate that of a patient with obstruction of the respiratory passages. There may be marked indrawing of the suprasternal spaces, the use of the accessory muscles of respiration in the neck and a marked retraction of the thoracic wall along the line of attachment of the diaphragm. For the apparent vigor of the effort made there seems to take place a surprisingly small movement of air as determined by auscultation.

In an attempt to determine what factors were present which were preventing the free ingress of air, we were brought to consider what effect the cohesion of the moist surfaces of the air passages and the alveoli in airless and collapsed lungs might have in resisting the initial distention. Experiments were devised to demonstrate such an effect and to measure it.

As occasion permitted, lungs of premature infants coming to necropsy and showing on examination in the gross extensive atelectasis, without infection or extensive hemorrhage, were removed with the trachea attached. Each such pair of lungs was suspended in a wide-mouthed

glass bottle which was made air-tight and connected to a source of suction, the degree of which could be varied at will (fig. 1). A suitable motor-driven valve rhythmically interrupted the suction and allowed the pressure to return to atmospheric pressure. The apparatus could thus be made to act like a miniature Drinker respirator. The trachea, by means of suitable tubing, was connected to the outside air. The suspended lungs inside the bottle could thus quite simply be subjected to an intermittent negative pressure of any magnitude desired, and the lung the connection of which with the outside air was still maintained could be observed as it rhythmically expanded and contracted within the bottle. Although nearly the same effect could be obtained by forcing air into the trachea under positive pressure, we were able by the use

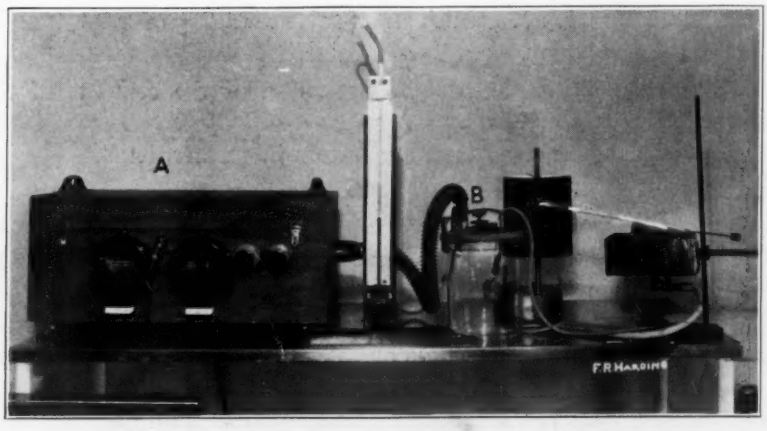

Fig. 1.—Apparatus for determining the distensibility of the lungs. *A*, power unit to furnish the source of the alternating suction. *B*, bottle respirator containing the distended lung shown in figure 2.

of the respirator to imitate exactly the mechanism of normal respiration when the entire lung distal as well as proximal to any obstruction is intermittently subjected to a negative pressure. Thus we could directly observe the lungs, which had felt atelectatic and which appeared macroscopically to be so, expand little by little while subjected to the rhythmically interrupted suction. The usual sequence in an extremely atelectatic lung as gradually increasing pressures were applied during successive "inspirations" was as follows: First a slight dilatation of the perihilar region would appear, then at unpredictable points a small peripheral area suddenly would expand and become pink; then more and more such areas would appear and coalesce till the lung was fully distended with each inspiration (fig. 2). The normal elasticity of the lung, even twenty-four hours post mortem, was adequate to bring

about almost complete contraction, passively, following each release of the pressure to that of the atmosphere. Thus no positive pressure was required to bring about "expiration."

Full expansion was not accomplished, however, without the use of considerable pressure, sometimes up to 35 cm. of water (from 13 to 16 cm. of water is the usual pressure effective in maintaining artificial

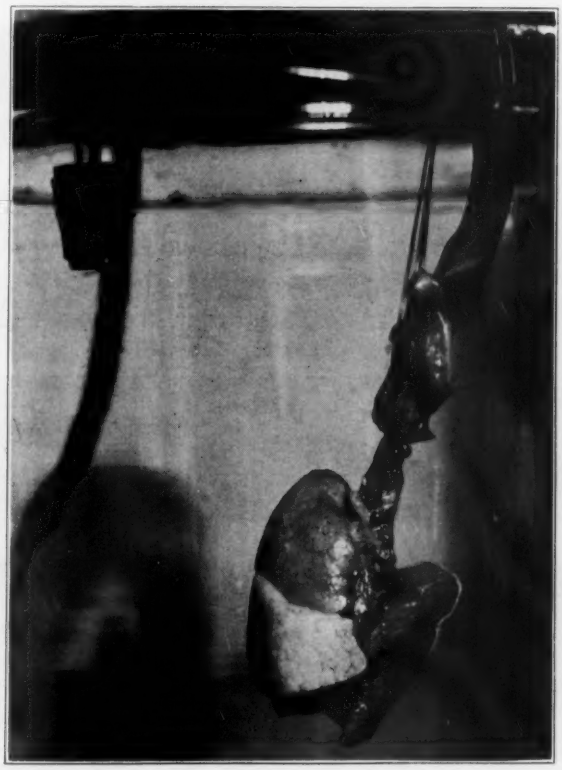

Fig. 2.—Photograph of the expanded lung taken through the wall of the bottle respirator. The lung on the right has been clamped off and is collapsed. The lung on the left shows the lower and middle lobes wholly expanded. The upper lobe is partially expanded. The picture was taken thirty hours post mortem, but the lungs were still air-tight and had maintained their elasticity.

respiration in the Drinker respirator, which is slightly greater than the usually recorded intrapleural pressure in quiet inspiration).

It was noted, however, that once the lungs had been distended much lower degrees of pressure were effective than were initially required.

A record was made of the degree of expansion of a lung when distended by a negative pressure in the respirator bottle. The trachea of the lung preparation, which was extended to the outside of the

bottle respirator by suitable tubing, was in turn connected to a small Krogh spirometer, the motion of which was graphically recorded (fig. 1). Any expansion of the lung in the apparatus caused a quantitatively comparable motion of the spirometer. The expansion of the lung when subjected to a unit pressure was a measure of its distensibility, and the graphic record of this expansion furnished quantitatively a comparative measure of the distensibility. The absolute amount of

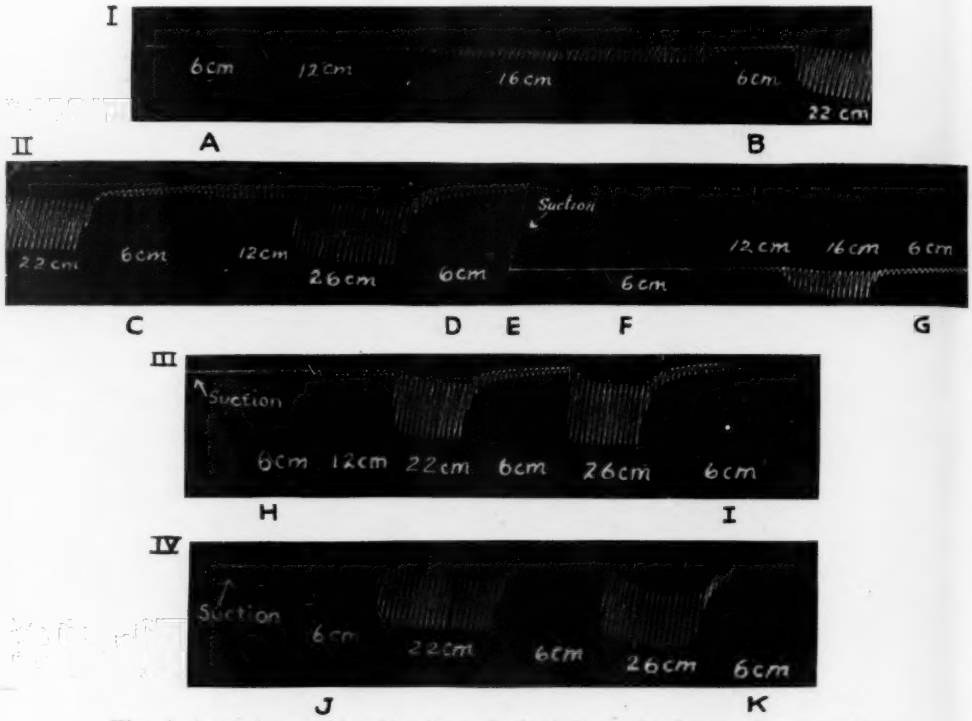

Fig. 3 (experiment A).—Tracings obtained from the lungs of a premature infant.

air exchange, though easily determinable, was of little significance in dealing with lungs of such variable size.

In general the program of experimentation was to obtain a record of the distensibility of the lung at a certain low negative pressure (intermittently applied as in actual respiration), to use a considerably higher pressure to produce greater expansion and finally to return to the original low pressure.

Many observations confirmed the impression that the initial effort required to distend a lung post mortem was much greater than was necessary after full distention had once taken place. A typical curve is shown in records *I* and *II* of experiment A (fig. 3). As can be seen,

although little motion of the lungs is at first recorded with low pressures, after higher pressure had once been used and the lungs had been expanded, a return to the original low pressure resulted in a considerable degree of expansion.

EXPERIMENT A (fig. 3).—The lungs of a 3½ pound (1,587.58 Gm.) premature infant were removed at necropsy and suspended in a bottle respirator (fig. 1), the trachea being connected to a small Krogh spirometer. Expansion of the lung caused a fall of the spirometer which was recorded on a kymograph. Intermittent negative pressures measured in centimeters of water were applied as indicated by the figures on the tracings (fig. 3), which show the relative distentions of the lungs produced by these pressures. At *A* no distention of the lungs occurred with a negative pressure of 6 cm. Compare with the distention at *B*, obtained with the use of 6 cm. of pressure after moderate distention by 12 and 16 cm. of pressure, and with the distention at *C*, obtained with the same low pressure after distention with 22 and 26 cm. of pressure. At *E* the lungs were completely collapsed by suction with a syringe attached to the trachea and were held collapsed for a few seconds. At *F* a pressure of 6 cm. produced only the slightest motion, but at *G* the lungs became more distensible following the use of 16 cm. of pressure. Records *III* and *IV* each show results obtained after the lungs were entirely collapsed by suction with a syringe. The lungs returned to their original state of distensibility each time. Compare the amplitude of the motion at *H* with that at *I* and the amplitude at *J* with that at *K*.

The phenomenon seemed easy of explanation. It seemed apparent that when the lungs were collapsed the moist surfaces of the air passages in contact became more or less adherent. A considerable force was required to overcome this cohesive tendency and to allow the entrance of air.

It was further noted, however, that if the lungs after being distended by the respirator were allowed to stand several hours, it was again necessary to use an initially great pressure to distend them.

The degree to which the expansibility of the lung became reduced on standing was variable, but the reduction always occurred to a certain extent and was usually marked. Whether the lungs were allowed to stand at ordinary room temperature or in the ice room at 34 F. made no constant difference. It was noted that the elasticity of the lungs as measured by the completeness of passive expiration after distention was little affected by standing as long as twenty-four hours at room temperature.

It was further noted that once a lung was well expanded, forceful contraction maintained by steady suction with a syringe attached to the intratracheal cannula would in a few moments reduce the lung practically to its original state, so that again the expansion of the lung per unit of pressure applied became initially greatly reduced. The finding was found consistently in many attempts (records *II*, *III* and *IV*, experiment A, fig. 3).

At first experiments were carried out on the lungs of premature infants only (twenty in number), and usually a considerable period (from three to fifteen hours) post mortem. The question arose as to whether the findings were essentially dependent on the excessive atelectasis of prematurity or whether the same results would be found in lungs which had been fully expanded in life. The influence of post-mortem changes needed also to be considered.

It was difficult to obtain for experiment the lungs of infants who had lived long enough for normal atelectasis to have disappeared and whose lungs showed no pneumonia. The lungs of most older children

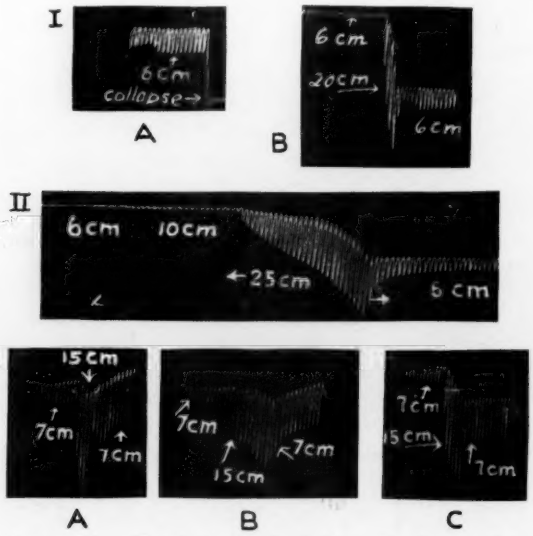

Fig. 4 (experiment B).—Tracings obtained from the lungs of a rabbit killed with paraldehyde.

and infants coming to autopsy show some pneumonia with inflammatory bronchial secretions which we wished to avoid.

Accordingly, the lungs of rabbits which had died following the intraperitoneal injection of sodium amytal were immediately removed and arranged without delay in the bottle respirator, or the entire animal was placed in a miniature Drinker respirator with a tracheal cannula connected with the spirometer. Findings similar to those in the lungs of premature infants were obtained. Experiment B (fig. 4) shows typical records. As can be seen, the same results were obtained in the freshly killed animal as in one examined several hours post mortem. The initial resistance of the lungs to expansion was, then, not due to postmortem changes or to any peculiarity in the atelectasis of the newborn infant's lung.

EXPERIMENT B (fig. 4).—The rabbit was killed with paraldehyde (intraperitoneal injection). The entire animal was placed in the respirator; the lungs were not removed. Tracheotomy was performed; a cannula was inserted and connected with the spirometer. The pressure in the respirator was measured in centimeters of water and recorded; records *I, II* and *III* show quantitatively the distentions of the lungs by the various pressures employed.

In record *I* (fig. 4) the lungs had previously been distended with the respirator. At *A* is shown the amplitude of the distention of the lung when subjected to an alternating negative pressure of 6 cm. The lungs were then collapsed by suction with a syringe attached to the trachea. In *B* is shown the effect after this collapse. Very little motion was obtained at first with 6 cm. of pressure. Then a force of 20 cm. was applied for a few breaths, and 6 cm. was again tried. The distensibility became markedly increased. (The fall in the curve when 20 cm. of pressure was used was due to a minute leak of air from the lungs at the height of inspiration.) It should be noted that these lungs were not removed from the thorax, which was intact. Many quite similar curves were obtained with lungs removed from the thorax when other rabbits were used.

Record *II* was obtained in a similar manner. Four hours elapsed between the two records. Much of the distensibility had disappeared, but after an application of 25 cm. of pressure a marked increase occurred. Compare the degree of expansion obtained by the use of 6 cm. of pressure before and after the application of 25 cm. of pressure.

Three short curves are shown in record *III*. The same procedure was carried out in each, and the same results were obtained. The entire dead animal was placed in the respirator, and the trachea was connected with a spirometer. Before each curve was obtained the lungs were completely collapsed by suction with a syringe attached to the trachea. Then an intermittent negative pressure was applied in the respirator first at 7 cm. of water pressure, then at 15 cm. and last at 7 cm. The expansibility of the lungs as measured by the degree of expansion for the unit of pressure applied became diminished each time by the forceful collapse and increased by the distention. Compare the amplitude of the curve at 7 cm. of pressure before and after the use of 15 cm. in each experiment.

It was possible, however, that the findings would be different in the living lung through which blood was circulating.

An attempt was made to reproduce the conditions in the living animal. Rabbits were anesthetized by the intraperitoneal injection of paraldehyde or of sodium amytal and placed in a miniature Drinker respirator. A tracheal cannula was inserted, a bilateral pneumothorax was created by extensive thoracotomy, and artificial respiration was instituted. At intervals, artificial respiration was stopped, and by forceful suction with a syringe attached to the tracheal cannula, the rabbit's lungs were quickly and completely collapsed. The trachea was then speedily connected to the spirometer, artificial respiration was again started, and records were made of the amount of distention produced by the various pressures used in the respirator. After a short interval the system was disconnected from the spirometer, and vigorous unobstructed respirations were again maintained in order to keep the animal alive. In this manner it was possible to carry out on the living

animal the same experiment as that performed on the lungs of premature infants obtained at necropsy and on the lungs of dead rabbits. Records *I* and *II* of experiment C (fig. 5) show typical tracings of such experiments. Although the distensibility was not reduced by the briefly maintained collapse to a point as low as could be brought about in the excised lung, a definite reduction was consistently obtained.

EXPERIMENT C (fig. 5).—The rabbit was anesthetized with an intraperitoneal injection of paraldehyde and placed in a small Drinker respirator. A tracheotomy was performed, and a tracheal cannula was inserted which was connected for short intervals to a Krogh spirometer. A bilateral thoracotomy was next performed with the animal in the respirator and an open pneumothorax created. The animal was thus entirely dependent on the respirator. Records of the animal's

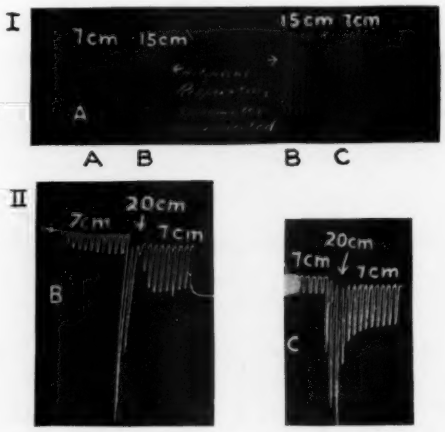

Fig. 5 (experiment C).—Tracings obtained from the lungs of a rabbit anesthetized with paraldehyde.

breathing were obtained before thoracotomy (not shown). Connection of the trachea and spirometer was made for short periods only in order to preserve the animal. Before connection of the rabbit's trachea to the spirometer a syringe was attached to the trachea, and the lungs were quickly and completely collapsed by forceful suction. Records were then obtained, and the comparative ventilation of the lungs with different negative pressures obtained in the respirator were measured in centimeters of water pressure.

In record *I*, note the expansion of the lung at *A* with a pressure of 7 cm. of water and compare with that at *C* with the same pressure. A pressure of 15 cm. was maintained at *B* (the spirometer was disconnected for a few moments to prevent the animal rebreathing the air in the spirometer). After the initial collapse, the lungs were only about half as distensible at *A*, before full expansion (*B*), as afterward at *C*.

In the same manner in record *II*, before *B* and again before *C*, the lungs of the living animal were completely collapsed by forceful suction with a syringe. In *B* and in *C*, as can be seen, between two applications of a negative pressure of 7 cm. the lungs were distended for a few cycles by a pressure of 20 cm. In *B*

the distensibility of the lung was at least doubled, and in *C* more than doubled, after the forceful inspirations. The animal's heart was beating well at the end of *B*, but only faintly after *C*.

It is believed that this initially lessened distensibility of the lungs after they have stood for several hours in a state of passive collapse or after they have been entirely exhausted of air by forceful suction is due to the cohesion of the moist surfaces of the air passages, and that this is an important factor in the maintenance of the fetal state of atelectasis after birth; it is a factor that is always present, and when combined with any of the other conditions to be discussed, it causes the state of atelectasis to persist to a pathologic extent.[2]

INEFFECTIVE ACTION OF THE RESPIRATORY CENTER

That there may exist a "central disturbance" which brings about ineffective thoracic expansion is generally recognized. There is still considerable controversy as to whether the normal chemical stimulus to the respiratory center exists in anoxemic new-born babies. It has long been maintained by Henderson [3] that such a stimulus is not present —a belief which he supported by the contention that the carbon dioxide content of the blood of asphyxiated new-born infants is abnormally low.

It has recently been demonstrated by Eastman,[4] however, that the hydrogen ion concentration in these babies is far greater than normal. With the modern conception of Gesell that the essential respiratory hormone lies in the metabolic processes of the nerve cell itself, it seems probable that a normally adequate stimulus to breathe is present, but that the respiratory center fails to respond to that stimulus owing to some pathologic state.

Dysfunction of the respiratory center due to inadequate development or to mechanical or asphyxial injury is highly probable in many cases. The irregularity of the breathing and the intermittent cyanotic attacks point to a central disturbance. There is ample pathologic evidence of gross injury to the medulla of new-born babies from hemorrhages. It

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2. Since this work was carried out, our attention has been called to the work of L. Hermann (Arch. f. d. ges. Physiol. **20**:365, 1879). He removed the trachea and lungs from a freshly killed rabbit and placed the lungs in a bottle filled with water. A screen at the mouth of the bottle prevented the lungs from rising and permitted the trachea to be connected to tubing. After repeated washing with carbon dioxide the lungs were collapsed and permitted to sink. Hermann found that a much larger pressure was required to expand such a collapsed lung initially than was necessary immediately thereafter. This phenomenon he explained on the basis of adhesion and stickiness of the bronchial walls.

3. Henderson, Y.: The Prevention and Treatment of Asphyxia in the New-Born, J. A. M. A. **90**:583 (Feb. 25) 1928.

4. Eastman, N. J.: Bull. Johns Hopkins Hosp. **47**:22, 1930; **48**:260, 1931; **50**:39, 1932.

is well recognized, moreover, that cerebral hemorrhage is especially frequent in premature infants, even when they have not suffered from what is ordinarily considered a traumatic delivery. Whether the faulty central control of respiration is brought about by injury or is due to inadequate development, it is obvious why the state of atelectasis existing in utero might persist to a pathologic extent in the absence of normal, initially vigorous and rhythmic respiration. An abnormal respiratory center may then be an acceptable cause of atelectasis.

UNDERDEVELOPMENT OF THE THORAX

Frequently the mechanical inefficiency of the breathing of a premature infant seems strikingly apparent. There may be marked indrawing of the suprasternal spaces, the use of the accessory muscles of respiration in the neck and a marked retraction of the thoracic wall along the line of attachment of the diaphragm. The last feature is often very impressive. The action of the diaphragm seems remarkably vigorous and out of all proportion to the small pulmonary air exchange as detected with the stethoscope. It seems apparent that much of the effect of the descent of the diaphragm, which tends to expand the thoracic cage, is offset by the marked retraction of the thoracic walls through the pull of the diaphragm, which in turn tends to diminish the volume of the thorax. It seems reasonable that an underdeveloped thorax with weak intercostal muscles and an elastic bony structure, which is seen especially in premature infants, may contribute in an important manner to the persistence of atelectasis.

OBSTRUCTION IN THE BRONCHIAL TREE

The clinical picture of extensive atelectasis is often strikingly like that produced by foreign body obstruction of the air passages, an impression frequently borne out by the localized diminution or absence of breath sounds.

Aspiration of infected or noninfected fluid or semifluid matter by the infant just before or during labor is an important factor in neonatal mortality (Johnson and Meyer [5]).

Small amounts of the contents of the amniotic sac are present in the lungs of every new-born infant, aspirated from the mouth and thorax with its first breath. As has been shown by Farber and Sweet,[6] aspiration of large amounts of the contents of the amniotic sac may cause marked respiratory obstruction. In such cases, the bronchioles, alveolar ducts and alveoli may be so filled with these contents, consisting

5. Johnson, W. C., and Meyer, J. R.: Am. J. Obst. & Gynec. **9**:3, 1925.

6. Farber, Sidney, and Sweet, L. K.: Amniotic Sac Contents in the Lungs of Infants, Am. J. Dis. Child. **42**:1372 (Dec.) 1931.

mainly of masses of vernix and cornified cells from the skin of the fetus, that respiration is greatly interfered with.

The following question then arises: Is such aspiration an important factor in maintaining the atelectatic state in the new-born, either full-term or premature, through simple bronchial obstruction?

Full-Term Infants.—In a series of one hundred full-term new-born babies, most of whom died within two days after birth, 15 per cent showed evidences of aspiration of large amounts of the contents of the amniotic sac with resultant secondary atelectasis. It is believed that much of the atelectasis in these cases (15 per cent) could be explained by bronchial obstruction due to aspirated contents of the amniotic sac. Although extensive atelectasis existed in many other cases in this series, bronchial obstruction due either to aspirated contents of the amniotic sac or to mucous plugs could not be demonstrated as an adequate cause.

Premature Infants.—In premature infants, however, aspiration of the contents of the amniotic sac is not so important a problem as in the full-term new-born baby. There are smaller amounts of vernix and a smaller number of cornified cells in the sac contents of such premature infants, since the cornification of the skin of the fetus and the production of vernix take place largely in the last months of pregnancy. Gross and microscopic examinations of the lungs of more than two hundred premature babies were made. The results as far as they bear on this question can be briefly summarized. On gross dissection of the bronchial tree, there was no evidence of plugging of the bronchi by mucus or other foreign material. On microscopic examination there was in many cases some evidence of the contents of the amniotic sac in the terminal bronchioles and alveolar ducts. In a few cases a large amount of this material was found, but not enough to account for more than a small part of the total atelectasis present.

Massive hemorrhage into the lungs or the aspiration of large amounts of regurgitated blood from the stomach must be mentioned as a cause of secondary atelectasis on the basis of bronchial obstruction. It is questionable whether petechial hemorrhages in the lungs or the presence of a few red cells in the alveolar walls can mechanically cause any significant amount of atelectasis in the premature infant, as suggested by Ylppö.[7] We have been able to study the lungs of more than thirty new-born babies in whom an effective barrier to the passage of air in parts of the lungs was occasioned by the presence of large amounts of blood in the bronchioles, alveolar ducts and alveolar spaces, but this

7. Ylppö, A., in Langstein, L.: Beiträge zur physiologischen, Pathologie und sozial Hygiene des Kindesalters, Berlin, Julius Springer, 1919.

finding could rarely explain more than a small part of the total atelectasis found.

In order to determine more directly by another method whether the atelectasis of premature infants was due to bronchial plugging which could not be overcome by a strong inspiration, a study was made of the results of inflation of the lungs after death.

As occasion permitted, the lungs of twenty premature babies coming to autopsy and showing gross evidence of atelectasis without extensive hemorrhage or evidence of pneumonia were placed in the bottle respirator (fig. 1). One lung was clamped off to act as a control, and progressively greater negative pressures were used until the other lung was apparently fully distended.

Except for occasional hemorrhagic areas or areas where masses of parenchymal cells not yet formed into alveoli existed, we found by gross and by histologic examination that practically all the lung could be completely distended by sufficient negative pressure, and that there existed a striking difference between the expanded side and the control side.

The control (unexpanded) lung showed the typical picture of atelectasis. It was deep bluish red, and the surfaces were smooth. No outlines of lobules were visible beneath the pleura. The consistency of this lung could best be compared to that of the thymus. No crepitus could be elicited. On section the cut surfaces were dull bluish red and uniform throughout all lobes, the sectioned vessels standing out as definite landmarks. The parenchyma of the lung had the structural appearance of thymus and differed only in color and amount of blood. A definite glandular pattern consisting of acinus-like structures could be recognized on the cut surfaces. No air could be expressed from the parenchyma on pressure.

The lung which had been artificially inflated was larger in size and varied in color from dull to pale salmon pink. Definite lobulations of air-containing structures could be seen throughout the pleura, and crepitus could be elicited (fig. 2). On section the cut surfaces were salmon pink, and the usual markings of a well expanded normal lung were present. Little of the ordinary type of atelectasis was left on the distended side, but areas of unexpandable pulmonary tissue often became more prominent by contrast. Histologically, there was often fairly marked emphysema. Distention of all the alveoli was thus not accomplished without overdistention of some. At times pressures as high as 35 cm. of water were used before full distention occurred. Pressures of 25 and 30 cm., however, usually brought about striking changes.

It could thus be concluded that in the atelectatic lungs of premature infants at necropsy, when gross infection or hemorrhage was not present, obstruction of the air passages rarely existed to such a degree

that it could not be overcome by forceful inspiration, and that all of the atelectasis commonly found in premature infants could be overcome by repeated forceful artificial inspiratory efforts.

CONCLUSIONS

We have pointed out that atelectasis in the new-born should not be considered a primary cause of death. Except in the lungs of the smallest premature infants, in which there may be found fairly extensive areas of undeveloped pulmonary tissue, the lungs of new-born babies are structurally perfect with well developed airways and alveoli. Persistent initial atelectasis of the new-born should be considered secondary and should not be accepted as, in itself, a complete explanation of the failure to thrive or of death.

We have shown by measurement of the resistance to expansion of the lungs of dead infants and of dead and living animals that the cohesion of the moist surfaces of the air passages in collapsed and airless lungs offers a considerable obstacle to the entrance of air, and that a relatively great force is required to overcome this cohesion and to separate the bronchial and alveolar walls during the initial expansion of an atelectatic lung. The first breath of a new-born baby may thus be its most difficult one. For a variable period after birth, especially vigorous inspirations must be maintained until the atelectasis is finally overcome.

This initial resistance of the atelectatic lungs to expansion which is always present may, when combined with other factors, maintain the state of atelectasis to a pathologic extent. The other factors may be considered under three heads:

1. An imperfectly developed or an injured respiratory center which, not responding to normal respiratory stimuli, fails to bring about repeated and sufficiently vigorous respiratory efforts. Evidences of immaturity of the central control of respiration in the brain stem may be detected in many premature infants. Damage to the medulla due to trauma, hemorrhage or direct asphyxia is a well known and frequent condition in the new-born.

2. An imperfectly developed thoracic mechanism such that the contraction of the intercostal muscles and the bony resistance of the thorax do not furnish an effective *vis a tergo* for the efficient action of the diaphragm. This is especially seen in premature infants.

3. Bronchial obstruction due to aspiration of the contents of the amniotic sac, mucus or blood. This we have shown may be of great importance in full-term infants, less frequently so in premature infants; only rarely is it, in itself, however, a complete cause of extensive and persistent atelectasis.

News and Comment

UNIVERSITY NEWS

The University of Colorado School of Medicine has appointed Drs. Roy Parsons Forbes and Emanuel Friedman as assistant professors of pediatrics and Drs. Roderick J. McDonald, Jr., and Wilford W. Barber as instructors in pediatrics.

The faculty of the Western Reserve University School of Medicine announces the promotion of Drs. James D. Pilcher and John A. Toomey to associate professors of pediatrics.

The St. Louis University School of Medicine announces the following promotions in the faculty: Dr. John Zahorsky to director of the department of pediatrics, and Dr. Julius A. Rosen to assistant professor in the same department.

Dr. E. Earl Moody has been appointed professor of pediatrics, College of Medical Evangelists, Los Angeles.

GENERAL

Bequests and Donations.—The Children's Memorial Hospital of Chicago has received $50,000 from the estate of Fred B. Jones.

The Zem Zem Hospital for Crippled Children of Erie, Pa., was willed $21,000 from the estate of Joseph A. Stern.

The New York Nursery and Child's Hospital was bequeathed $10,000 from the estate of John Markle, and $50,000 under the will of the late Mrs. Mary Mildred Hammond Sullivan.

DEATHS

Prof. Leo Langstein of Berlin died on June 7, at the age of 57. For many years previous to his death Professor Langstein had been director of the Empress Auguste Viktoria House in Berlin. He was born in Vienna and was an early assistant of Heubner's. Langstein was one of the outstanding pediatricians, and was associated with a group of young men who began after 1900 to distinguish themselves and their specialty in Germany. His loss will be keenly felt.

Doc. Dr. Bohuslav Feierabend, director of the Division of Sera of the Federal Health Institute at Prague, was killed with his wife and two daughters, by an avalanche, in the Dachstein Mountains on July 6, 1933. Dr. Feierabend was one of the primary group of Rockefeller exchange physicians sent to the United States for postgraduate study. His American training included that in the laboratories of the New York Board of Health, the biologic division at Washington and several commercial organizations. Under his direction the institute has grown so that it is able to supply the serums and vaccines needs of the whole of Czechoslovakia.

Pediatric Biographies

PERCIVALL POTT
1713–1788

JOHN RUHRÄH, M.D.
BALTIMORE

Percivall Pott, whose name is known to medical students because of its use in three different conditions, was born on Jan. 6, 1713 (1714?), in London in a house in Threadneedle Street, where the Bank of England now stands. At 7 years of age he was sent to school at Darenth in Kent, and at 16 years of age he was apprenticed to Mr. Nourse, surgeon to St. Bartholomew's Hospital. For this apprenticeship, which lasted seven years, 210 pounds was paid. In 1736, he was given a diploma by the Barbers' and Surgeons' Company. He then took a "business" in Fenchurch Street and was apparently successful, for he was elected an assistant surgeon to St. Bartholomew's, and five years later was one of its principal surgeons. He removed to Bow Lane and married Sarah Cruttenden. In 1756, he fell from his horse and sustained a compound fracture of the leg. Remembering the ill results from rough handling, he had a rough litter made from a door and poles from a sedan chair. He narrowly escaped having his leg amputated, but it was saved by the intervention of his old preceptor. Previous to his accident he had published but one paper, but while he was convalescing and subsequently he was a rather prolific writer.

In 1765, he started a course in anatomy and surgery. A few years later he took a house near Lincoln's Inn Field. In 1787, after having served nearly half a century, he resigned his position at the hospital, and the occasion of his leave-taking was marked by a meeting at which his life and works were extolled. He died on Dec. 22, 1788, from pneumonia. His last conscious words were, "My lamp is almost extinguished: I hope it has burnt for the benefit of others." He was buried in Aldemary Church, Bow Lane.

He was awarded various honors during his life. In 1764, he was elected a fellow of the Royal Society; in 1786, the Royal College of Surgeons of Edinburgh gave him an honorable diploma, the first one granted. In 1765, he was elected a governor of the Barbers' and Surgeons' Company.

Pott's fracture is that of the lower third of the fibula with an outward displacement of the foot. "Puffy swelling" of the head was once known by Pott's name, while Pott's disease is the paralysis of the legs caused by spinal caries. Pott wrote on congenital hernia and engaged in a controversy on the subject with William Hunter.

Pott's chief pediatric contribution appeared in 1779 and was called "Remarks on That Kind of Palsy of the Lower Limbs Which is Frequently Found to Accompany a Curvature of the Spine, and is Supposed

PERCIVALL POTT, F.R.S.
1713–1788

to be Caused by It, Together with Its Method of Cure." This was followed about three years later by "Farther Remarks on the Useless State of the Lower Limbs in Consequence of a Curvature of the Spine." These are 40 and 48 pages, respectively, as printed in his collected works. The articles are too long to quote, but a few excerpts will be of interest.

> The disease of which I mean to speak, is generally called a palsy; as it consists in a total or partial abolition of the power of using, and sometimes of even moving the lower limbs, in consequence, as is generally supposed, of a curvature of some part of the spine.

To this distemper both sexes, and all ages, are equally liable. If the patient be an infant, it becomes an object of constant, though unavailing distress to its parents; if an adult, he is rendered perfectly helpless to himself, and useless to all others, which, of all possible states, is surely the very worst.

When this disease attacks an infant of only a year or two old, or under, the true cause of it is seldom discovered until some time after the effect has taken place, at least not by parents and nurses, who know not where to look for it. The child is said to be uncommonly backward in the use of his legs, or it is thought to have received some hurt in its birth.

When it affects a child who is old enough to have already walked, and who has been able to walk, the loss of the use of his legs is gradual, though in general not very slow. He at first complains of being very soon tired, is languid, listless, and unwilling to move much, or at all briskly; in no great length of time after this he may be observed frequently to trip, and stumble, although there be no impediment in his way; and whenever he attempts to move briskly, he finds that his legs involuntarily cross each other, by which he is frequently thrown down, and that without stumbling; upon endeavoring to stand still and erect, without support, even for a few minutes, his knees give way and bend forward. When the distemper is a little farther advanced, it will be found that he cannot, without much difficulty and deliberation, direct either of his feet precisely to any exact point; and very soon after this, both thighs and legs lose a good deal of their natural sensibility, and become perfectly useless for all the purposes of locomotion. When an adult is the patient, the progress of the distemper is much the same, but rather quicker.

Until the curvature of the spine has been discovered, it generally passes for a nervous complaint; but when the state of the back bone has been adverted to, recourse is almost always had to some previous violence to account for it; some pulling, lifting, carrying, or drawing a heavy body, which is supposed to have hurt the back. In some few instances, this exertion may have been such, as might be allowed to have been equal to the effect; but, in by much the majority, this is so far from being the case, that if it be admitted to have had any share at all in it, some predisposing cause, at least, must be looked for, in which (in my opinion) consists the very essence of the disease. . . .

The curvature of the spine, which is supposed to be the cause of this complaint, varies in situation, extent and degree, being either in the neck or back, and sometimes (though very seldom) in the upper part of the loins; sometimes comprehending two vertebrae only, sometimes three, or more, by which the extent of the curve becomes necessarily more or less; but whatever may be the number of vertebrae concerned, or whatever may be the degree or extent of the curvature, the lower limbs only feel the effect—at least I have never once seen the arms affected by it. . . .

While the curvature of the spine remains undiscovered or unattended to, the case is generally supposed to be nervous, and medicines so called are most frequently prescribed, together with warm liniments, embrocations, and blisters, to the parts affected; and when the true cause is known, recourse is always had to steel stays, the swing, the screw chair, and other pieces of machinery, in order to restore the spine to its true and natural figure; but all, as far as I have observed, to no real or permanent good purpose; the patient becomes unhealthy, and, languishing for some time under a variety of complaints, dies in an exhausted, emaciated state; or, which is still worse, drags on a miserable existence, confined to a great chair, or bed, totally deprived of the power of locomotion, and useless both to himself and others. . . .

The remedy for this most dreadful disease consists merely in procuring a large discharge of matter, by suppuration, from underneath the membrana adiposa on each side of the curvature, and in maintaining such discharge until the patient shall have perfectly recovered the use of his legs. . . .

From the whole, the few following practical inferences seem fairly deducible:

1. That the disease does not originally consist in a displacement of the vertebrae, made by violence, the bones and ligaments being previously in a sound and uninjured state; but in such a morbid alteration of the texture of both, as will, if not timely prevented, produce curvature and caries, with all their consequences.

2. That the proper remedies for this disease cannot be applied too soon.

3. That the restoration of the spine to its natural figure, depends much on the early administration of the help proposed.

4. That although the distemper may be so far cured, that the patient may perfectly recover the use of his legs, yet such an alteration may have taken place in the bodies of the vertebrae, as to render it impossible for the spine to become straight again.

5. That when three or four, or more vertebrae, are concerned in the curve, the trunk of the body will have so little support from that part of the spine which is not distempered, that no degree of deformity can be wondered at; nor can it be expected that such deformity should be removed, whatever other benefit such patient may receive.

6. That if from inattention, from length of time, or from any other circumstances, it happens that the bodies of the vertebrae become completely carious, and the intervening cartilages are destroyed, no assistance is to be expected from the proposed remedy.

Pediatrics in Art

INFANTILE ALCOHOLISM

JOHN RUHRÄH, M.D.
BALTIMORE

The effects of alcohol afford many an artist material. Luca Giordano (1605-1705), the Neapolitan, a pupil of Ribera, sometimes got away from the religious subjects which made him famous and portrayed

Baccanale.

scenes like the Baccanale. The effects of alcohol need not be commented on, but the central figure shows one of its chief consequences, sleep, while the other have "their wine-driv'n brains, involv'd in follie's cloud." Milton in "Comus" uses the apt phrase "From out the purple grape crushed the sweet poison of misused wine."

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

HERPETIC INFECTION OF THE CHORIO-ALLANTOIC MEMBRANE OF THE CHICK EMBRYO. JAMES R. DAWSON, JR., Am. J. Path. **9**:1 (Jan.) 1933.

The chorio-allantoic membranes of the chick embryo are susceptible to infection with a strain of herpes simplex virus which is innocuous to adult chickens of the same breed. The microscopic lesions of these membranes are like those of herpetic lesions of mammals. A peculiar nuclear change in ectodermal cells is described, characterized by enormous enlargement of the nucleus and by a partitioning of it by delicate trabeculae into compartments which are filled by minute, uniform and faintly stained basophilic granules.

AUTHOR'S ABSTRACT.

BONE LESIONS IN RATS PRODUCED BY THE SUBSTITUTION OF BERYLLIUM FOR CALCIUM IN THE DIET. SHELDON A. JACOBSON, Arch. Path. **15**:18 (Jan.) 1933.

The Steenbock diet 2965, with the addition of cod liver oil but without calcium, produced osteoporosis but not rickets in young rats. Animals fed in exactly the same way with the addition of beryllium carbonate contracted a disease anatomically indistinguishable from rickets. Young rats given a diet of fatty meat and cod liver oil showed extreme osteoporosis, and in them also the administration of beryllium carbonate resulted in rachetoid lesions.

LEMASTER, Evanston, Ill.

HISTOLOGIC CHANGES IN RABBITS AND DOGS FOLLOWING THE INTRAVENOUS INJECTION OF THORIUM PREPARATIONS. EVAN SHUTE and M. EDWARD DAVIS, Arch. Path. **15**:27 (Jan.) 1933.

By the use of thorium salts the spleen and liver of rabbits and dogs could be outlined, but visualization of the placenta in pregnant animals was unsuccessful. The authors advise strongly against the use of thorium in clinical work because of the marked degeneration of the spleen and liver seen in the experimental animals. In one rabbit thorium caused abortion and spontaneous rupture of the spleen. The placenta contained only small amounts of thorium a few days after its administration and prevented any thorium from reaching the fetus.

LEMASTER, Evanston, Ill.

DISSOCIATION AND SENSITIVENESS TO NORMAL SERUM IN DYSENTERY BACILLI OF TYPE III. T. THJOTTA and E. WAALER, J. Bact. **24**:301 (Oct.) 1932.

Since Sonne described dysentery bacilli of type III, in 1915, it has been known that these microbes may form peculiar colonies, which show a picture different from that presented by the colonies of the other types of dysentery bacilli. Sonne called attention to the fact that this type is especially liable to form variants, which, he supposes, is the reason why it so often shows irregularities of agglutination.

The authors have found that dysentery bacilli of type III produce both S and R colonies in the first culture from the stool. The S colonies are very unstable, while the R colonies are found in all laboratory strains of this type of dysentery bacilli. The reason for the low titers of agglutination in serums both from patients and from animals after immunization formerly described is that the R type of the bacillus and not the S type has been used. The reason why dysentery bacilli of type III have been found to be exceptionally sensitive against normal active serum is to be found in the fact that the R type of this microbe is very

sensitive to normal serum. This is not the case with the S type of the same microbe, which is resistant against the serum that will dissolve the R type. As the R type always has been dealt with in bactericidal tests, the characters of this type have erroneously been thought to be those of the species.

STOESSER, Minneapolis.

EFFECT OF MASSIVE AND REPEATED DOSES OF BACTERIOPHAGE. N. W. LARKUM and RUTH CORPRON, J. Bact. **25**:77 (Jan.) 1933.

The authors gave rabbits inoculations of staphylococcus bacteriophage as follows: daily injections of 2 cc. each, intravenously, for twenty-five doses; daily injections of 2 cc. each, subcutaneously, for twenty-five doses; a single injection of 50 cc., intravenously, and a single injection of 50 cc. subcutaneously. The reaction in the rabbit was followed by making records of the temperature and weight and by frequent blood counts. The question of increased susceptibility to staphylococcic infection was investigated. After a brief period of rest all of the rabbits were given massive intravenous injections of living staphylococci. The mortality of the experimental animals as compared with that of the controls shows a marked degree of protection. Some indication is given as to the relative efficiency of single large versus multiple small inoculations and as to the choice of routes of inoculation.

STOESSER, Minneapolis.

OBSERVATIONS ON THE ELEMENTARY BODIES OF VACCINIA. JAMES CRAIGIE, J. Bact. **25**:79 (Jan.) 1933.

The author says that the elementary bodies of vaccinia represent the virus of vaccinia. They may be isolated from the skin of the rabbit and washed free from the Seitz-filtrable precipitable substance. Vaccinia virus has been transmitted in series through more than twenty rabbits, washed elementary bodies being employed as the inoculum throughout. Over 20 cc. of washed elementary body suspension sufficiently potent to give a confluent take in a 1:100,000 dilution and sufficiently dense to permit of macroscopic agglutination tests in dilutions of from 1:20 to 1:50 may be obtained from a single rabbit.

In previously vaccinated rabbits the inoculation of dead washed elementary bodies causes an increase of agglutinins commensurate with that produced by the injection of living elementary bodies. The early reaction following revaccination in adults has been elicited as readily with dead washed elementary bodies as with heated calf virus.

STOESSER, Minneapolis.

STUDIES OF LOCAL REACTIVITY TO THE BACTERIAL TOXINS. AUGUSTUS WADSWORTH and GRACE M. SICKLES, J. Bact. **25**:80 (Jan.) 1933.

From the point of view that the phenomena of local reactivity in the experiments of Arthus, of Sanarelli and of Shwartzman are fundamentally similar and are obviously manifestations of the action of foreign poisons as determined by different phases of tissue susceptibility, a series of experiments was undertaken by the authors with different pathogenic bacteria and their products. The results indicated some of the conditions of tissue susceptibility which were essential to the activity of bacterial toxin.

With the technic of Shwartzman, little or no local hemorrhagic response was elicited when the products of the diphtheria bacillus were injected either intradermally or intravenously. The observation was confirmed that hemorrhagic reactions may be obtained in areas of the skin of rabbits previously prepared with filtrates of known potency when products of streptococcus growth are injected intravenously. With the pneumococcus, reactions were obtained only in rabbits in which a dermal infection was induced and type-specific pneumococci were recovered at autopsy. Intravenous injections of bacterial filtrates of known reactivity, of 0.2 per cent agar and, occasionally, of heavy suspensions of killed pneumococci induced these reactions.

From the results obtained in these experiments with the pneumococcus, the following technic was developed to determine conditions under which bacterial products that were inactive became active: Rabbits sensitized to serum were inoculated intradermally with bacterial products, such as bile-lysed pneumococci, pneumococcus carbohydrate and streptococcus toxin, or with live bacteria. Twenty-four hours later, 1 cc. of horse serum was injected intradermally in the same area, and twenty-four hours after that injection an intravenous dose of meningococcus toxin was given. In some animals a marked hemorrhagic reaction appeared before the intravenous dose was given. In the remaining animals the intravenous inoculation was followed within five hours by marked hemorrhagic changes in the edematous area.

STOESSER, Minneapolis.

STUDIES ON VARIABILITY OF C. DIPHTHERIAE. LLOYD R. JONES, J. Bact. **25**:97 (Jan.) 1933.

A typical culture of virulent Corynebacterium diphtheriae grown in broth or on agar mediums at 45 C. irregularly gave rise to the development of several variant types, as follows: Type A, a temporary variant, differing from the parent type only in exhibiting markedly granular colonies, irregular in contour, which were unstable, readily reverting to the parent colony type. Type B, a hereditary variant, permanently avirulent but similar to the parent type in all other discernible characteristics. Type C, a temporary variant, regularly avirulent, differing markedly from the parent strain in colonial form by exhibiting a small transparent colony; practically devoid of fermentative ability, and exhibiting pleomorphism in smear preparations ranging from small coccoid to elongated solid-staining and occasionally granular types. This variant was unstable, showing a tendency toward partial reversion to the parent type colony under ordinary conditions of cultivation. Type D, a hereditary variant similar to type C and derived in stable, pure-line strains through many consecutive re-isolations incident to persistent cultivation under the cultural conditions employed to incite the transformation. Similar type D variants were obtained incident to cultivation of the parent culture in broth containing specific antibacterial serum or phenol or lithium chloride. The properties which characterize this variant type, regardless of manner of derivation, have remained constant in cultures maintained over periods of from six months to two years.

Some experiments of the author also indicate antigenic dissimilarity between the virulent parent type organism and its avirulent variants.

STOESSER, Minneapolis.

THE DETOXIFICATION OF POLLEN ANTIGENS. GEORGE E. ROCKWELL, J. Bact. **25**:100 (Jan.) 1933.

The author states that desensitization of persons with hay fever by hypodermic injections of pollen extract is not entirely satisfactory because it is often attended with from mild to severe reactions. Hence, the dosage cannot be increased very rapidly. If such a pollen antigen could be treated so that it would not give these reactions, and still be potent for the prevention of hay fever, there would be a distinct improvement.

Ragweed pollen extract was oxidized by treatment with hydrogen dioxide. The hydrogen dioxide was then removed by the use of platinized asbestos. This oxidized pollen extract gave little or no cutaneous reaction when sensitive persons were tested.

Such oxidized ragweed pollen antigen was used in the treatment of three patients with hay fever. There were no reactions, and hence the dosage could be increased much more rapidly than it could have been if regular ragweed pollen extract had been used. The clinical results were very satisfactory.

STOESSER, Minneapolis.

THE SPECIFICITY OF URINARY PROTEOSE. R. S. STEEL, M. J. Australia **2**:800 (Dec. 31) 1932.

Steel reports his inability to duplicate the findings of Oriel and Barber regarding the specificity of urinary proteose.

GONCE, Madison, Wis.

AGE VARIATIONS IN SUGAR METABOLISM AFTER ADMINISTRATION OF PHLORHIZIN. M. NAGATAKE, J. Pediat., Tokyo, Oct. 20, 1932, no. 389, p. 1972.

The author found that the blood sugar normally is higher in young than in older rabbits. Phlorhizin causes hypoglycemia in rabbits. When administered by the subcutaneous route, phlorhizin causes hypoglycemia in equal degree in young and in old animals, but the younger the animal, the more rapid is the change. When the substance is given by the oral route, the young animal shows an opposite effect from that produced in the mature one. No convulsive symptoms were noted even in the presence of such low blood sugar values as from 0.027 to 0.030 mg. per hundred cubic centimeters.

KATO, Chicago.

THE EFFECT OF CARBON TETRACHLORIDE ON THE BLOOD AND ITS AGE VARIATIONS. Y. TAKEDA, J. Pediat., Tokyo, Oct. 20, 1932, no. 389, p. 1988.

Repeated injections of carbon tetrachloride cause the following changes: There are a decrease in the erythrocytes and an increase in the reticulocytes. Anemia is more marked in mature animals, while reticulosis is more marked in young animals. Repetition of injections causes also an increase in the fragility of washed corpuscles, more marked in mature than in young animals. The antihemolytic action of plasma against saponin is greatly increased in mature animals, while not so noticeable in young ones. The cholesterol content of whole blood is increased more in mature animals than in young animals, and the same is true of serum bilirubin. The total serum protein decreases slightly in mature animals, while the opposite effect is found in immature ones. The serum globulin tends to decrease in both young and mature animals.

KATO, Chicago.

Nutrition

DEPRESSION OF INTESTINAL REDUCTION BY VITAMIN D. LESTER YODER, Ann. Rep. Iowa Agric. Exper. Stat., 1931, p. 51.

Vitamin D apparently causes a change in the digestive processes of the intestinal tract whereby the utilization of combined oxygen in ferric oxide in a ration deficient in vitamin D is decreased. This may be due to a decrease in the reducing products of intestinal digestion or to a substitution of a better source of oxygen for their neutralization or oxidation through the vitamin. Probably both of these phenomena are involved when vitamin D is added to rickets-producing rations for rats.

KUGELMASS, New York.

VALUE OF MEATS FOR GROWTH, REPRODUCTION, LACTATION AND HEMOGLOBIN FORMATION IN ALBINO RATS. P. MABEL NELSON and PEARL P. SWANSON, Ann. Rep. Iowa Agric. Exper. Stat., 1931, p. 90.

Comparison of the concentration of hemoglobin in the blood of rats fed a basal ration having lean meat as the protein constituent with that in rats raised on a mixed cereal ration showed that beef greatly increased the concentration of hemoglobin. Pork fed in addition to autoclaved yeast produced the highest level of hemoglobin of any of the diets studied. The incidence of anemia cannot be correlated with the consumption of pork.

KUGELMASS, New York.

INFLUENCE OF EXPERIMENTAL TECHNIC DURING THE PRELIMINARY DEPLETION PERIOD IN VITAMIN A DETERMINATIONS. P. MABEL NELSON and PEARL P. SWANSON, Ann. Rep. Iowa Agric. Exper. Stat., 1931, p. 90.

In order to determine the factors influencing gain in weight and vitamin A depletion in rats, the statistical method was applied to the data on 469 tests with vitamin A feeding. There is a possible difference in the reactions of rats fed vitamin A-free diets containing different amounts of fat. The data showed also that the quantity of basal ration ingested was the measured variable having the greatest percentage effect on the gains in weight of the animals. A vitamin A-free diet containing fat is preferable to a fat-free basal diet, as it shortens the time required to deplete the body store of vitamin A. Homogeneity of the rat colony is essential in research on vitamin A.

KUGELMASS, New York.

THE ULTRA-VIOLET ABSORPTION SPECTRA OF CERTAIN VITAMIN B-CONTAINING PREPARATIONS. FRANCIS F. HEYROTH and JOHN R. LOOFBOUROW, Bull. Basic Sc. Research **3**:237, 1931.

The absorption spectra of two vitamin B concentrates prepared by Seidell and of one prepared by the authors have been determined. They resemble those of purines and pyrimidines investigated and previously reported on by the authors. They show somewhat greater resemblance to the spectra of certain purine and pyrimidine irradiation products, especially if the irradiation is carried out with ultraviolet rays from which the shorter waves have been excluded. There is evidence to show the presence of purine-containing or pyrimidine-containing compounds, or modifications thereof similar to those brought about by irradiation with ultraviolet rays, in vitamin B concentrates.

KUGELMASS, New York.

THE INFLUENCE OF BRAN ON THE ALIMENTARY TRACT. MARY S. ROSE, GRACE MACLEOD, ELLA MCC. VAHLTEICH, ESTHER H. FUNNELL and CATHERINE L. NEWTON, J. Am. Dietet. A. **8**:133 (July) 1932.

In studies on healthy women, the laxative effect of bran was as satisfactory the second month as the first. Two tablespoons of bran proved laxative in 50 per cent of the cases in which it was given daily to thirty-eight girls in institutions where the diet was adequate. Rats fed for from two to four months on doses of bran large enough to be laxative showed no signs of pathologic lesions of the intestinal tract. It is suggested that the addition of bran to diets low in vitamin B caused a laxative effect from the combined effect of fiber and Vitamin B.

LEMASTER, Evanston.

THE TREATMENT OF RACHITIC INFANTS WITH MILK PRODUCED BY COWS FED IRRADIATED ERGOSTEROL. HENRY J. GERSTENBERGER and ARTHUR J. HORESH, J. Nutrition **5**:479 (Sept.) 1932.

Two infants having rachitis as judged by chemical and roentgen evidence were fed 500 cc. of whole milk daily. In addition they received 500 cc. of skim milk, 5 cc. of lactic acid and 15 cc. of orange juice and a sufficient amount of carbohydrate to meet their caloric requirements. The whole milk was supplied by cows which were fed daily 100 mg. of irradiated ergosterol having an antirachitic value of 200,000 rat units.

The treatment periods were for ten and eleven weeks, respectively. Weekly roentgenograms and biweekly determinations of the blood serum calcium and phosphorus were made. The results indicate that "the milk possessed antirachitic powers but that these were not of great magnitude.

It is estimated that a pint of this particular milk contained slightly less than the equivalent of a half teaspoonful of cod liver oil having a rat protective potency of 5 mg. per day.

MUNNS, Winnetka, Ill.

GROWTH PROBLEMS AND THEIR RELATION TO ZONES OF NORMAL PHYSIOLOGIC REACTIONS. WILLIAM PALMER LUCAS, HELEN BRENTON PRYOR, CRAWFORD BOST, SAXTON T. POPE and MARION C. HENDERSON, J. Pediat. **1**:572 (Nov.) 1932.

In this study, the authors apply a simple statistical technic to clinical data and correlate the findings. The body type of a child is found by dividing the width of the pelvis by the height. The average indexes in 3,400 cases arranged according to age and sex are listed. The necessity of considering the child's body type before passing judgment on his nutrition as compared to height-weight tables is demonstrated. The metabolic rate was determined in 573 children from 3 to 18 years of age. The normal zone of variation of the basal metabolic rate of preschool children was found to be from 0 to + 20 per cent. A prepubescent rise in metabolism was not seen. Many children with complaints such as fatigue and susceptibility to infections were found to show basal metabolic rates well outside the normal, and marked improvement in symptoms followed correction of metabolic variation. Roentgenograms taken for bone age were thought to be of material assistance in determining skeletal status and progress in growth. The Schneider tests for exercise tolerance proved of value in confirming the diagnosis of fatigue and cardiac difficulties and also in estimating improvement and outlining treatment. Of 184 children with anorexia, 82 per cent were of the linear body type. Personality studies showed that an unusually large percentage of children from 6 to 9 years of age were considered "highstrung," probably owing to the starting of school work. The shape of the head was found to depend more on the body type of the child than on his intelligence.

LEMASTER, Evanston, Ill.

A CRITICAL CLINICAL STUDY OF CONCENTRATED AND DRIED INFANT FOODS: II. MODIFIED DRIED MILK. ADOLPH G. DESANCTIS, JOHN D. CRAIG and OLIVER L. SPRINGFIELD, J. Pediat. **1**:704 (Dec.) 1932.

A group of 117 infants was fed on a dried milk preparation, consisting of whole cow's milk with added cream and lactose. The authors believe that the high fat content is of decided benefit. All of the infants took the milk mixture well. The normal infants gained 5.44 ounces per week and the marantic infants gained 5.4 ounces per week. There were only four gastro-intestinal disturbances in the series. The incidence of rickets was no higher than in infants fed on other milk modifications. It is suggested that this milk is of value as a concentrated food for marantic infants. Children do well if fed on this preparation for a year or even longer.

LEMASTER, Evanston, Ill.

NUTRITIVE VALUE OF STRAINED VEGETABLES IN INFANT FEEDING. GEORGE W. CALDWELL, J. Pediat. **1**:749 (Dec.) 1932.

The value of vegetables in the diet of infants from the standpoint of furnishing vitamins, minerals and nutritive ingredients is discussed. Among sixty infants strained canned vegetables were fed in amounts of 1 ounce (31 Gm.) daily to those under 3 months of age, 2 ounces (62 Gm.) to those from 3 to 5 months old and 4½ ounces (140 Gm.) daily to those over 5 months old. The vegetable feedings were well tolerated and well digested; the infants developed very satisfactorily. The importance of vegetables in promoting proper development of teeth and bone in infancy is emphasized.

LEMASTER, Evanston, Ill.

A COMPARATIVE STUDY OF INFANT FOODS. ROGER H. DENNETT and JOHN DORSEY CRAIG, M. J. & Rec. **136**:133 (Aug. 17) 1932.

The authors fed 443 infants successfully on four different kinds of milk. Those on artificial feedings were fed according to their caloric requirements, the breast-fed babies being nursed at four hour periods, their appetite thus being permitted to be the sole guide to their caloric requirements. The authors used a powdered

milk, modified cow's milk and evaporated milk; they found more intestinal indigestion and diarrhea among breast-fed infants than among those fed on modified cow's milk, powdered milk or evaporated milk.

The average weekly gain was about the same among the breast-fed infants and those fed modified cow's milk, but considerably less than that of those fed evaporated milk and powdered milk.

The carbohydrates used in the study were cane sugar, dextrin, lactose and corn syrup. Lactose was found to have an advantage over the others, as the infants that were fed lactose gained more.

WILLIAMSON, New Orleans.

DIET, NUTRITION AND INFECTION. ALFRED F. HESS, New England J. Med. **207**:637 (Oct. 13) 1932.

This is an interesting résumé of the rôle played by the vitamins, particularly fat-soluble A, in combating infections, especially those of the upper respiratory tract. Systematic use of ultraviolet rays from the mercury vapor arc or carbon arc lamps, cod liver oil and special certified raw milks with high vitamin content all failed to cause an appreciable decrease in infections of the upper respiratory tract. Even children with carotinemia (carotin is regarded as the provitamin of vitamin A) showed no decrease in these infections. Children suffering from xerophthalmia and night blindness (due to lack of vitamin A) showed no increased susceptibility to infections of the upper respiratory tract, but showed an increase in infections of the skin such as impetigo and boils.

Hess stresses the important rôle played by age in the incidence of infections in institutional children. A ten year survey (1916-1927) showed the following incidence of pneumonia (case rate per age group): 0 to 6 months, 4.3; 6 to 12 months, 13; 1 to 2 years, 15.4; 2 to 3 years, 8; 3 to 4 years, 3.1; 4 to 5 years, 1; or an average case rate of 7.3 in a child population of 6,894 during the decade. As the store of vitamin A is apparently insignificant at birth, the decreased rate in the first six months cannot be explained on that basis.

A further check with aseptic nursing and a large cubicle system proved the correctness of the assumption that age has an influence on the incidence of infections in the upper respiratory tract. The fatality rate, however, was higher in the younger group.

There is also an interesting table of the "number of infections in relation to age among infants receiving cod liver oil or viosterol" by three month periods up to eighteen months. This corroborates the findings by age groups and incidentally shows that the average number of infections per infant per month in all groups was: those receiving cod liver oil, 0.26; viosterol, 0.18.

Attention is again called to the "widespread occurrence of nasal diphtheria in infantile scurvy," and evidence is offered that a lack of vitamin C may induce a heightened local susceptibility to infection of the respiratory tract, with the suggestion that this may possibly be true of vitamin A also. However, Hess leaves the rather definite impression that the administration of increased amounts of vitamin A does not decrease the incidence of infections of the upper respiratory tract in infants and young children.

GENGENBACH, Denver.

REPORT OF COMMITTEE ON MILK CONFERENCE OF STATE AND PROVINCIAL HEALTH AUTHORITIES, JUNE 2, 1932, Pub. Health Rep. **47**:1686 (Aug. 12) 1932.

The use of the term "natural milk" should not be permitted for either raw or pasteurized milk. The use of short time, high temperature pasteurization is approved under the restrictions recommended by the United States Public Health Service, dated February, 1932. If more than one grade of milk is sold by a distributor, separate equipment and a separate location must be maintained for each grade of milk. The practice of recombining surplus skimmed milk and cream is condemned unless the product is so labeled. Educational measures are recom-

mended to increase the percentage of pasteurized milk for sale in smaller cities and towns. Cooperation between state health and agricultural departments concerning milk problems is discussed.

LeMaster, Evanston, Ill.

Rickets: A New Treatment. Preliminary Report. James Bloom, South. M. J. **25**:1109 (Nov.) 1932.

On the basis of chemical data, the author concludes that the calcium and phosphorus content of cow's milk is not available for complete metabolism, owing perhaps to the large amount of both of these elements which is encased in the curd.

He considers it more than likely that the p_H of the gastric content plays a part in rickets, and that an increase in the acidity may facilitate the absorption of the calcium and phosphorus.

The type of milk given probably plays a part in the utilization of dicalcium phosphate.

The addition of secondary calcium phosphate may supply an excess of both calcium and phosphorus and thereby replace the amount of calcium and phosphorus contained in the curd, which apparently is not available.

The author also believes that the addition of secondary calcium phosphate to milk can prevent and cure rickets without the aid of vitamin D.

Schlutz, Chicago.

The Relative Vitamin A and Vitamin D Contents of Samples of Cod-Liver Oil. Katherine H. Coward, F. J. Dyer and Barbara G. E. Morgan, Analyst **57**:368, 1932.

For many years the "blue value" of cod liver oil, as obtained by the action of antimony trichloride on it, has been considered as an approximate measure of the vitamin A content. Examination of some thirty samples of oil showed, however, that this color value is no indication of the vitamin D potency. Examination of seventeen samples showed that a high blue value is usually associated with a high vitamin A value, but oils having the same color value are often quite different with respect to vitamin A potency. The vitamin D values are also not proportional to the vitamin A values.

Kugelmass, New York.

Vitamin Content of Australian, New Zealand and English Butters. M. E. F. Crawford, E. O. V. Perry and S. S. Zilva, Medical Research Council, Special Report Series, no. 175, London, His Majesty's Stationery Office, 1932.

The content of vitamins A and D in numerous samples of butter from Australia, New Zealand and England was determined and found to be as high as the vitamin content of the best butter available from any source. The vitamin D content of New Zealand butter was lower in the winter than in the summer, but the vitamin A content showed no seasonal variation. Cold storage for from five to ten months caused no decrease in vitamin potency, but after two years a noticeable decrease was demonstrated. The vitamin potency of the butter was approximately the same for various breeds of cows and for the various districts of Australia. Neutralization of acid creams before churning did not destroy either vitamin A or D. There is also presented a short historical survey of the vitamin A and D content of butter and a detailed description of the methods used in the analysis of the vitamins in this study.

LeMaster, Evanston, Ill.

Phosphorus Balance of Rats on a Rachitogenic Diet Rich in Calcium, Strontium or Magnesium. Andree Roche, Bull. Soc. chim. biol. **14**:634, 1932.

Young rats weighing from 50 to 100 Gm. were put on a rachitogenic diet (Pappenheimer 85) low in phosphorus. They became rachitic at first but usually

recovered after from twenty-five to thirty days. During this period the phosphorus balance was practically zero. When 2 per cent of strontium carbonate was added to the same diet, the phosphorus balance was negative, and remained so until death. Some rats lost 50 per cent of the total phosphorus of the body in six months. Somewhat similar results were obtained when 2 per cent of calcium or magnesium carbonate was added to the diet. The possible existence of phosphorus reserves in the body is discussed.

KUGELMASS, New York.

DIARRHEA IN BREAST-FED INFANTS. A. B. MARFAN, Paris méd. **2**:366 (Nov. 5) 1932.

After ruling out congenital syphilis and a neuro-arthritic constitution, Marfan believes that the diarrhea occasionally seen in breast-fed infants in the first three months of life is an allergic reaction. He treats this condition with belladonna and with bismuth.

SANFORD, Chicago.

TREATMENT OF INFANTILE DIARRHEA BY FRUIT. M. SCHACHTER, Progrès méd., Nov. 26, 1932, p. 2018.

Besides apples, apricots, pears and bananas may be used. To a 14 month old child the author gave six bananas on the first day of a diarrheal disturbance; complete amelioration of the symptoms resulted in forty-eight hours.

SANFORD, Chicago.

THE VITAMIN CONTENT OF DRIED FIGS AND DATES. MUHIDDIN ALI, Arch. f. Hyg. **107**:219, 1932.

A diet consisting only of dried figs or dates is associated with an immediate loss of weight and cannot be continued long without harm. Dried dates contain only a little vitamin B, and no A, C or D. Dried figs are relatively rich in vitamin A, contain vitamin B in moderate amounts, very little vitamin D and possibly traces of vitamin C. In the author's experiments, in feeding the test animals the dates were given without the pits, while the seeds were present in the figs. This corresponds, however, to the way in which these foods are used in the human diet. The vitamin content of fresh figs and dates was not studied.

GLASER, Rochester, N. Y.

MAGNESIUM CONTENT OF MAN. E. BECHER and K. HAMANN, Deutsches Arch. f. klin. Med. **173**:500 (July 25) 1932.

By the authors' method, normal blood serum was found to contain an average of 2 mg. of magnesium per hundred cubic centimeters. Patients without renal disease ordinarily showed a slight reduction in the serum magnesium, although those with jaundice showed a slight increase. Renal disease without renal insufficiency was associated with no increase in magnesium in the serum, but in most cases in which insufficiency was present it was associated with a definite increase which, however, did not parallel the degree of insufficiency. In contradistinction to calcium, magnesium is present in the erythrocytes in higher concentration than in serum. In spinal fluid and muscle tissue there is more magnesium than calcium. In the brain and the liver, the magnesium content is high in proportion to that of blood serum.

DOOLEY, Kent, Conn.

PRESENT STATUS OF THE PROBLEM OF BREAST FEEDING. WALTHER FREUND, Ergebn. d. inn. Med. u. Kinderh. **40**:136, 1931.

It is generally accepted that most maternal diseases — such as diabetes, epilepsy, psychoses, anemia following severe hemorrhage and puerperal fever — constitute only a relative contraindication to nursing, unless they are of a particularly severe grade. There is division of opinion as to maternal open tuberculosis as an absolute

contraindication to nursing. Finkelstein, Lederer, Bessau and Grosser consider it an absolute contraindication; Meyer, Nassau, Moll, Czerny, Keller, Pfaundler and the author take a relative position on this question. Almost all writers consider erysipelas, diphtheria, grip and pertussis absolute contraindications to breast feeding. It is also generally agreed that a mother who contracted syphilis just before delivery should under no circumstances nurse her baby, and that babies free from syphilis who are born of recently infected mothers should not be nursed or should be nursed with great care. In psychic disturbances of the mother, it is necessary to act with care. Menache reported twelve cases of lactation psychoses which cleared up as soon as the babies were removed from the breast and recurred partly when lactation was resumed.

The author warns against overfeeding the mother as a means of stimulating milk secretion; he cites the experiences during the war and postwar period, when the mothers of Germany were definitely undernourished and yet the formation of milk was not disturbed. Mention is also made of the view of practically all German pediatricians that nursing mothers may eat anything, and that no article in their diet should be excluded because it might influence unfavorably the milk and hence the nursing infant.

The author adds his own observations on 124 cases to those of Engel, showing that mothers who secrete little milk begin to menstruate early, even from four to six weeks after delivery, and Engel concludes that the lowered secretion of milk is not the result but the cause of the early return of the menses.

The causes of nutritional disturbances in breast-fed infants are alimentary, constitutional and infectious. Since the establishment of the five feedings a day schedule, overfeeding as a cause of nutritional disturbances in breast-fed infants is rapidly disappearing; underfeeding, however, still plays a frequent rôle. Lederer subdivides the cases of nutritional disturbance due to underfeeding into two classes, those of the "quiet sufferers" and those of the "rebellious;" the former are characterized by ominous stillness and pseudo-obstipation, and the latter by diarrhea, vomiting and marked unrest.

In addition, the author reviews the subjects of pseudohypogalactia, galactagogues, the diet of the nursing mother, technical problems of breast feeding, difficulties in breast feeding, complementary feeding and wetnursing. This discussion is chiefly a review of well known existing views on the subjects with an occasional personal comment by the author.

CAPPER, Philadelphia.

EFFECT OF VITAMIN D ON THE NONRACHITIC ORGANISM. F. THOENES, Jahrb. f. Kinderh. **131**:1 (March) 1931.

Controlled experiments showed that rats on a diet low in fat developed keratomalacia and infections when given large doses of irradiated ergosterol. These symptoms were prevented to some extent by the administration of a fat low in vitamin A (margarine), and to a greater extent by that of butter fat.

CLAUSEN, Rochester, N. Y.

NUTRITION EXPERIMENTS WITH YOUNG GOATS: EFFECT OF AUTOCLAVED MILK AND VITAMINS B, C AND D ON GROWTH. W. CATEL and G. PALLASKE, Jahrb. f. Kinderh. **131**:313 (May) 1931.

Kids fed autoclaved milk of cows do not thrive, but die of cachexia, without signs of tetany. Irradiated ergosterol, from 20 to 40 drops per day, administered to such animals, causes normal growth. Yeast extract sometimes does.

CLAUSEN, Rochester, N. Y.

CAROTENE AND VITAMIN A. E. GLANZMANN, Jahrb. f. Kinderh. **133**:129 (Oct.) 1931.

This article consists of a review of the literature and of the report of experiments of the author which showed that carotene in daily quantities of from 5 to

10 Gm. causes considerable growth in rats fed a diet low in vitamin A. In such experiments, vitamin B is necessary, although better growth occurs if vitamins C and D are added. Lemon juice contains no vitamin A, but permits a better utilization of vitamin A reserves. Carotene should not be mixed with the food or with powders, as it is readily oxidized; it is best given dissolved in peanut oil, separately from the food. Carotene, from 5 to 10 Gm. a day, may cure early xerophthalmia. Large doses of carotene did not produce any symptoms referable to hypervitaminosis. The blood platelets are lowered when vitamin A is withheld, and rise promptly when carotene is administered. Anemia was also observed. The lowering of resistance to infection may be due in part to the lowering of the blood platelets.

CLAUSEN, Rochester, N. Y.

DEMONSTRATION OF TOXIC SUBSTANCES IN THE MILK OF LACTATING MOTHERS DURING MENSTRUATION. ERICH ELTZ, Jahrb. f. Kinderh. **136**:82 (June) 1932.

During menstruation, the milk of lactating women is toxic to germinating lupine seeds. This effect is also observed at regular intervals of three or four weeks, even before uterine bleeding has reappeared.

CLAUSEN, Rochester, N. Y.

HUNGER HYPOGLYCEMIA OF INFANCY: II. LACTIC ACID OF THE BLOOD. HERBERT SCHÖNFELD, Jahrb. f. Kinderh. **136**:173 (July) 1932.

After a fast of four hours, the values for blood sugar in twenty infants averaged 80 mg. and the lactic acid, 11.6 mg. per hundred cubic centimeters. After a further sixteen hour fast, these values were respectively 11.6 and 19.9. The inorganic phosphorus showed only a slight fall.

CLAUSEN, Rochester, N. Y.

EXPERIMENTAL RICKETS IN RATS. HIMA STOLZBERG and GEORG MEYER ZU HORSTE, Monatschr. f. Kinderh. **54**:195, 1932.

In metabolism experiments on rats made rachitic by the McCollum diet no. 3413 and cured while on the same diet by ultraviolet radiation, the writers found that in the beginning stages the phosphorus retention diminishes rapidly while the calcium also falls, but more slowly. This corresponds to findings reported by others in the rickets of infants. In the healing stages, however, calcium retention improved more rapidly than that of phosphorus. This is a variation from human rickets, as in the latter phosphorus metabolism seems to be the first to improve.

In the healing of rickets, there is a definite diminution in the excretion of minerals in the stool with some increase in the urine. Whether the diminished intestinal excretion is due to increased absorption of calcium and phosphorus or to a diminished excretion from the healing bones is not certain.

GERSTLEY, Chicago.

EXPERIMENTAL RICKETS IN RATS. GEORG MEYER ZU HORSTE, Monatschr. f. Kinderh. **54**:203, 1932.

In animal experimentation, the writer found that the addition of magnesium carbonate to a nonrachitic diet containing calcium and phosphorus in the proper proportions produces rickets in rats, due to a low phosphorus content, as does an excess of calcium carbonate. This rickets differs in no way histologically from the rickets induced by a low phosphorus diet. Magnesium rickets is accompanied by a diminution in blood phosphorus. It likewise is healed by ultraviolet irradiation, viosterol and cod liver oil.

As this form of rickets seems to resemble human rickets, the writer urges that one must not be satisfied with the relations of calcium to phosphorus in the diet, but that one should consider the relation of the combined calcium and magnesium to phosphorus.

GERSTLEY, Chicago.

VITAMIN A AND GROWTH ACTION OF EGG YOLK. HANS VON EULER and ERIKA KLUSSMAN, Ztschr. f. physiol. Chem. **208**:50, 1932.

The ethereal extract of egg yolks, after saponification and removal of sterols by digitonin, showed absorption bands in the ultraviolet area at 345 and 375 millimicrons. A mixture of 70 per cent xanthophyll and 30 per cent zeaxanthin showed a maximum absorption at 589 millimicrons and general absorption from 660 upward; addition of a vitamin A preparation produced two bands at 622 and 584 millimicrons and further addition of indole in chloroform left only the 584 millimicron band.

KUGELMASS, New York.

SYMBIOSIS AND ANTAGONISM OF PATHOGENIC BACTERIA AND THE NONPATHOGENIC FLORA IN MILK. A. DOSKOCIL, Časop. lék. česk. **70**:517 (April 10) 1931.

The author checked the effect of various milk flora on typhoid, paratyphoid, diphtheria and pyogenic streptococci. Milk soured by the natural lactic acid-forming organisms of milk may be considered generally free from pathogenic bacteria. In the review of the literature some observers cite typhoid as viable in soured fresh, that is, unboiled, milk after forty-eight days. B. lactis-aerogenes inhibits growth of typhoid, paratyphoid and the cocci, but is symbiotic for prolonged periods with the bacillus of Loeffler. Refrigerated raw milk may harbor pathogenic bacteria, and should be used only when collected from clean cows by clean milkers and handlers and should preferably be consumed locally. Boiled milk may be contaminated secondarily. This is especially true of milk products, which must be especially protected from possible typhoid or paratyphoid contamination. Boiled milk curdled by proteolytic bacteria is unfit for either human or animal consumption; it may contain bacteria and noxious byproducts.

STULIK, Chicago.

DETERMINATION OF VITAMIN A AND D. POUL SCHULTZER, Dansk. tidsskr. f. farmacol. **5**:177, 1931.

As a criterion for the action of vitamin A the optimal rate of growth and cure of xerophthalmia was used. The effective curative rat dose of vitamin A is the smallest number of milligrams of a material which must be given daily for from eight to ten weeks in order to effect a cure. The vitamin A content of a material is the number of rat doses contained in 1 Gm. of the substance. Vitamin D was determined by the preventive method, that is, the quantity of substance that would prevent rickets in young rats fed on McCollum's rickets-producing diet. The effective preventive rat dose of vitamin D is the smallest number of milligrams of a material which prevents rickets in young rats fed on McCollum's formula 3143. The content of vitamin D in a substance is the number of rat doses in 1 Gm. of the material.

KUGELMASS, New York.

VARIATION OF SERUM CALCIUM WHEN THERE IS NO FOOD INTAKE. R. NICOLAYSEN, Norsk mag. f. lægevidensk. **93**:774 (July) 1932.

The serum calcium may stay fairly constant when there has been no intake of food, but it has also been found by the author to vary considerably during twenty-four hours. Thus a variation of 2 mg. per hundred cubic centimeters was found in one experiment.

TOVERUD, Oslo, Norway.

Prenatal Conditions

THE FREQUENCY OF ANOMALOUS RETICULA IN THE RIGHT ATRIUM OF THE HUMAN HEART "CHIARI NETWORK." REPORT OF EIGHT CASES. FERDINAND C. HELWIG, Am. J. Path. **8**:73 (Jan.) 1932.

A typical Chiari network was found in eight cases, or 1.5 per cent of those in which routine autopsy was performed. It is suggested that this lesion is not

as rare as is usually supposed, since it is very delicate and easily broken by careless manipulation during the opening of the heart. No clinical symptoms could be correlated with the presence of the network. MOORE, Charlotte, N. C.

STUDIES ON THE PATHOLOGY OF DEVELOPMENT: II. SOME ASPECTS OF DEFECTIVE DEVELOPMENT IN THE DORSAL MIDLINE. N. W. INGALLS, Am. J. Path. **8**:525 (Sept.) 1932.

The dorsal midline is an area which is especially vulnerable to defects of development. On the dorsum of the head the region over the anterior rhombencephalon and midbrain is most affected, probably owing to inherent factors for growth and not to external influences. There are predisposing and exciting factors in maldevelopment. These factors are subject to great variation, and the variation and vulnerability are essentially germinal in character. There may be associated defects of the membranes which influence the maldevelopment. Some defects do not influence the gestation, others may give complete or adequate *restitutio ad integram*, and finally others cause irreparable damage. The author describes in detail seventeen specimens illustrating the aforementioned conditions.

MOORE, Cleveland.

CONGENITAL ATRESIA OF THE ESOPHAGUS: CASE REPORT. MARCY L. SUSSMAN, Am. J. Roentgenol. **26**:894 (Dec.) 1931.

The author reports the usual esophageal atresia with anastomosis of the lower pouch with the trachea because of the complete preoperative, postoperative and postmortem roentgen study. Photographs of the postmortem preparation and the roentgenograms are presented. Autopsy revealed atresia of the esophagus, with communication of the distal portion with the trachea, patent ductus arteriosus, patent foramen ovale, congestion of the liver and status after gastrostomy.

STULIK, Chicago.

ABSENCE OF HALF OF THE DIAPHRAGM: THORACIC STOMACH; DIAPHRAGMATIC HERNIA. EDWARD L. JENKINSON, Am. J. Roentgenol. **26**:899 (Dec.) 1931.

The literature reveals six cases of thoracic stomach and the author's case, which was discovered roentgenologically in a man of 68 years. A brief review of diaphragmatic hernia shows that this lesion is mostly left-sided, and may vary from only a small opening to absence of half of the diaphragm, which may be compatible with life. Thoracic stomach and diaphragmatic hernia may also be acquired after injuries due to crushing. In the patient whose case is reported the outstanding symptom was inability to take much food at a time without vomiting and frequently the sensation that the food lodged in his throat.

STULIK, Chicago.

CALCIFICATION OF THE MYOCARDIUM IN A PREMATURE INFANT. MORTIMER DIAMOND, Arch. Path. **14**:137 (Aug.) 1932.

In a premature infant (born at the twenty-sixth week) who lived for thirty minutes after birth, extensive calcification of the myocardium was found. The calcification was thought to be secondary to toxic degeneration of the muscle fibers. A review of forty-one cases of calcification of the myocardium reported in the literature shows that the process is secondary to necrosis of the muscle fibers caused by vascular, inflammatory or toxic conditions.

LEMASTER, Evanston, Ill.

CONGENITAL ATRESIA OF THE ESOPHAGUS WITH TRACHEO-ESOPHAGEAL FISTULA: CLINICAL ASPECTS. ALEXANDER H. ROSENTHAL and URIUS HIMMELSTEIN, Arch. Pediat. **49**:444 (July) 1932.

The writers report eight cases of congenital atresia of the esophagus with tracheo-esophageal fistula and review the literature on this subject. They believe

this condition to occur more frequently than is generally believed. The clinical picture of this congenital anomaly is described, as well as the procedures useful in diagnosis.

WADDELL, University, Va.

THE METABOLISM IN PREGNANCY: IX. THE FOETAL INFLUENCE ON THE BASAL RATE. ALLAN WINTER ROWE and WILLIAM CLOUSER BOYD, J. Nutrition **5**:551 (Nov.) 1932.

Rowe and Boyd believe that the usual increased metabolic rate during the last six months of gestation is not due solely to the fetal metabolism. In order to reach this conclusion, they analyzed the heat production of seventy-seven women during the last six lunar months of normal pregnancy. They concluded that the excess heat production is the result of a complicated and unknown mechanism engendered by the state of pregnancy but involving other factors than those of the growth of fetal tissue alone.

MUNNS, Winnetka, Ill.

INTRA-UTERINE FRACTURES. A. S. HALL, Proc. Roy. Soc. Med. **25**:1228 (June) 1932.

The patient was a girl of 10 weeks, whose birth was normal, no abnormality being noticed at that time. Since birth she had had a cough. Physical examination revealed retraction of the left side of the chest with impairment of note and breath sounds. The roentgenogram showed deformity extending from the fourth to the eighth ribs on the left side. The report is accompanied by a roentgenogram. The mother stated that when she was seven months pregnant she fell on her abdomen.

WILLIAMSON, New Orleans.

THREE CASES OF FAMILIAL CONGENITAL CYSTIC DISEASE OF KIDNEY AND LIVER. REGINALD LIGHTWOOD and G. H. LOOTS, Proc. Roy. Soc. Med. **25**:1230 (June) 1932.

Four children in the same family were known to have suffered from disease of the liver. Three of them had been admitted into the hospital under the author's care.

Peter, the third in the family, died at 1 year and 10 months of age, of fibrosis of the liver with cystic changes and a cystic condition of the kidneys. Details of the disease and the autopsy are given in the report. A sister, aged 4 years, showed evidence of hepatic disease and had slight albuminuria, and a brother, aged 2 years, also showed signs of hepatic disease, enlarged kidneys and albuminuria. Their cases are also given in the report.

WILLIAMSON, New Orleans.

FUSION OF MIDDLE-THIRD OF THE FIRST AND SECOND RIBS. DAVID LEVI, Proc. Roy. Soc. Med. **25**:1233 (June) 1932.

A boy, aged 8 years, was seen by the school physician and referred to the hospital because of the presence of a lump at the inner end of the first rib on the right. The roentgenogram showed fusion of the first and second ribs in the middle third on the right side. The condition appears to be congenital and is rare. No instance of this condition has been recorded in anatomic textbooks.

WILLIAMSON, New Orleans.

PSEUDO-HERMAPHRODITISM. DAVID LEVI, Proc. Roy. Soc. Med. **25**:1234 (June) 1932.

At birth the patient was registered as a girl. At 18 months of age, the child was brought to the hospital to determine the sex. The penis was stunted, and hypospadias of the urethra was present. The scrotum was cleft, and there was

well marked development of pubic hair. Examination of the abdomen gave negative results. The author believed that the child was probably a male with a complicating pituitary suprarenal tumor. If the latter proves to be present, the child may be a female.

WILLIAMSON, New Orleans.

TRUE ANOPHTHALMOS AND APPARENT ANOPHTHALMOS IN A NEW-BORN INFANT. E. REDSLOB, Ann. d'ocul. **169**:433 (June) 1932.

Redslob states that in the last eighty years approximately one hundred cases of anophthalmos have been reported. In most of the cases of so-called anophthalmos a rudimentary eyeball has been found in the orbital tissues. In consequence of this in the great majority of cases described as instances of anophthalmos the condition is in reality extreme microphthalmus. Only six cases have been reported in which microscopic examination of serial sections revealed no trace of the eyeball. Redslob reports the seventh case; this and the case described by Ovio are the only cases in which this rare malformation was well developed in a newly born infant. In their cases complete anophthalmos existed on the left side only. The right orbit contained a rudimentary eyeball. From the careful histologic study of his cases Redslob draws interesting deductions in regard to the pathogenesis of anophthalmos.

BERENS, New York. [ARCH. NEUROL. & PSYCHIAT.]

A CASE OF PLEONOSTEOSIS. E. FEIGUINE and S. TIKHODEEFF, Arch. de méd. d. enf. **35**:644 (Nov.) 1932.

A rare instance of congenital symmetrical bony deformity in a Russian boy, aged 14, was studied through a period of three years. While difficult to classify, it compared in all essential features with cases of maldevelopment of the osseous system described by Léri in which hypertrophy of certain elements in the skeletal system, principally the epiphyses, provoked ankylosis and resulting limitation of movement in both small and large articulations in the upper and lower extremities. In the case under discussion, gross abnormalities existed in the shoulder, elbow, knee and especially the radiocarpal articulations and the joints of the hand. In every instance, these deformities were bilateral. An attempt is made to trace the condition etiologically to a general dysfunction of the endocrine system.

AMESSE, Denver.

CONGENITAL DIAPHRAGMATIC HERNIA. TRILLAT and BELLY, Bull. Soc. d'obst. et de gynéc. **21**:278 (April) 1932.

A girl weighing 3,450 Gm. was delivered normally at term. The heart sounds during labor were normal. Immediately after delivery the infant cried, made several irregular inspirations and became rapidly cyanotic, and the respirations, which were somewhat like hiccups, gradually ceased. The heart outlines could not be percussed, but the cardiac pulsations, which were very irregular and weak, could be felt just outside the right nipple. A congenital malformation was suspected. Death occurred shortly afterward, and a very large diaphragmatic hernia, the contents of which filled the left thoracic cavity, was found. This was the second case of congenital diaphragmatic hernia observed in one year, and the two cases occurred in a series of 2,180 deliveries.

GLASER, Rochester, N. Y.

ANOMALY IN IMPLANTATION OF A SUPERNUMERARY THUMB. MARCEL LAPASANT, Rev. d'orthop. **19**:237 (May) 1932.

In the majority of instances, the supernumerary thumb articulates with the head of the first metacarpal. In the instance reported, there was a new articular facet about midposition on the diaphysis of the first metacarpal.

RYAN, Vancouver, B. C.

Acute Infections

CONVALESCENT SERUM IN THE PREVENTION OF MUMPS. MENDEL ZELIGS, J. Pediat. **1**:727 (Dec.) 1932.

Forty-four boys ranging in age from 10 to 18 years, who according to their history had never had mumps, were each given an injection of 5 cc. of convalescent's serum seven days after exposure to the disease. Mumps did not develop in any of these boys. It would appear from this report and from the data cited in the literature that convalescent's serum is of definite value in the prevention of mumps in exposed persons if employed early and in sufficient dosage.

LEMASTER, Evanston, Ill.

THE RELATION OF BOVINE MASTITIS TO HUMAN INFECTION. PAUL B. BROOKS, J. Prev. Med. **6**:111 (March) 1932.

Brooks states that in the cow susceptibility to mastitis apparently increases with age, Streptococcus mastitides being the most frequent incitant, and that while it is evident that under ordinary conditions these organisms are not pathogenic for man, experience shows that organisms not infective for man, when present in milk in sufficiently large numbers, may with their toxins be responsible for severe toxic disturbances affecting large numbers of persons, especially children.

Tuberculous infection, Brucella abortus infection, milk-borne septic sore throat and scarlet fever and gastro-enteritis are discussed.

The author concludes that pasteurization is the only practical safeguard, as careful methods and inspection of dairying are insufficient to afford adequate protection.

TURNER, Chicago.

PERMANENCY OF THE MILD TYPE OF SMALLPOX. CHARLES V. CHAPIN and JOSEPH SMITH, J. Prev. Med. **6**:273 (July) 1932.

The mild type of smallpox is thought to have had its origin, in this country, in Florida in 1896. It is fully as mild now as when it appeared thirty-five years ago. The germ must have been transferred from one person to another more than eight hundred times, yet it has bred true. Chapin and Smith have examined a great deal of statistical matter and conclude that there is no evidence that the mild strain has ever reverted to the classic type, that is, that the pathogen of the disease has ever undergone a mutation in that direction.

TURNER, Chicago.

THE ESSENTIAL PATHOLOGY FOUND IN DIPHTHERIA, SCARLET FEVER AND TUBERCULOSIS WITH SPECIAL REFERENCE TO INVOLVEMENT OF THE HEART, BASED ON REVIEW OF NECROPSY CASES AT THE BOSTON CITY HOSPITAL FOR THE PAST FORTY YEARS. RALPH L. IRWIN, New England J. Med. **207**:863 (Nov. 17) 1932.

In cardiac lesions in diphtheria, the myocardium, the conduction bundle or the nerves supplying the heart may be involved. Cardiac involvement occurred in approximately one fifth of the fatal cases of diphtheria.

The most important cardiac lesion is myocarditis. The muscle shows fatty degeneration, hyaline degeneration or necrosis. Muscle tissue once destroyed does not regenerate. Endocarditis and pericarditis (usually due to streptococci) occur in less than 2 per cent of cases.

Cardiac lesions in scarlet fever are uncommon. They include pericarditis which is usually associated with pleuritis, streptococcus endocarditis in less than 2 per cent of cases and, very rarely, myocarditis, of either the toxic or the infectious type.

The cardiac lesions in tuberculosis are pericarditis and, rarely, miliary involvement of the myocardium. Congenital malformations are said to predispose to cardiac involvement.

GENGENBACH, DENVER.

HEART IN DIPHTHERIA AND SCARLET FEVER. EDWIN H. PLACE, New England J. Med. **207**:864 (Nov. 17) 1932.

The frequency of involvement of the heart is from 3 to 5 per cent in the author's cases of diphtheria, averaging 4.3 per cent in the past five years. There is little difference in the incidence at different ages. The fauces and nasal vault are the chief sources from which these toxic damages arise. In no cases located solely in the larynx or below, in this series, has any injury to the heart resulted.

The onset of diphtheritic carditis is from the sixth to the twenty-first day after the beginning of diphtheria. As a rule, the earlier the onset, the graver is the prognosis. The first cardiac change is the softening and shortening of the first sound, and the diastolic pause is usually shortened. The blood pressure falls. The electrocardiograph is the only means of determining the exact nature of the disturbance of the mechanism. In some cases, the electrocardiograph has demonstrated a high degree of heart block. Patients presenting heart block show a high mortality. Death may occur within twenty-four hours after the onset of appreciable damage to the heart. The average time is about three days.

The mortality from diphtheritic heart damage is between 50 and 60 per cent. The highest death rate occurs between 1 and 2 years of age, when it is close to 100 per cent. From the ages of 2 to 10 years it is about 50 per cent, and in the adults in this series about 25 per cent. No case of cardiac damage has appeared in patients receiving antitoxin during the first twenty-four hours and such damage occurred rarely when antitoxin was used during the second twenty-four hours.

A number of case reports with electrocardiograms are given in detail.

The characteristic form of cardiac damage in scarlet fever is a benign endocarditis. In recent years this occurred in less than 0.1 per cent of the cases, while in earlier periods it was present in from 0.25 to 0.5 per cent. The diagnosis is based on the usual findings of fever, cardiac murmurs with tachycardia, changes in the size of the heart and associated arthritis. The onset is typical during the second and third weeks after the onset of scarlet fever. The course is usually favorable, and it is rare to find active disease persisting more than a few weeks. A series of cases, now being studied and extending back over several years, does not show great frequency of recurrent attacks.

GENGENBACH, Denver.

CURRENT PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES (JULY 17 TO AUGUST 13, 1932). Pub. Health Rep. **47**:1813 (Sept. 2) 1932.

The number of reported cases of poliomyelitis (395) was more than twice the number for the preceding period of four weeks, about the usual seasonal increase. Meningococcus meningitis showed a slight increase. With typhoid fever, the incidence has been higher than during the corresponding periods of the past four years. The incidence of scarlet fever has been increased over last year. Measles has dropped 70 per cent from the previous period of four weeks, a slower decline than usual. Influenza remained at the ordinary summer low level. Diphtheria was slightly more prevalent than last year, but considerably below the average for preceding years. The incidence of smallpox has been only from one-fourth to one-half that of the past few years.

LEMASTER, Evanston, Ill.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES, AUGUST 14 TO SEPTEMBER 10, 1932. Pub. Health Rep. **47**:1975 (Sept. 30) 1932.

The death rate of 9.4 per one thousand population for this four week period is the lowest in the seven years for which records are available. The incidence

of poliomyelitis has been increased in the Atlantic coast states and in the north central group. Measles, smallpox, diphtheria and meningococcus meningitis continue at low levels. The incidence of scarlet fever and influenza is slightly higher than in recent years, while typhoid fever is considerably more prevalent.

LeMaster, Evanston, Ill.

Current Prevalence of Communicable Diseases in the United States, October 9 to November 5, 1932. Pub. Health Rep. **47**:2217 (Nov. 25) 1932.

The incidence of diphtheria and of measles showed the expected seasonal increase. The number of cases of scarlet fever and influenza was definitely increased over the corresponding period in recent years. Poliomyelitis, meningococcus meningitis, smallpox and typhoid were reported to have a considerably lower incidence than is usual. The mortality from all causes was 10.3.

LeMaster, Evanston, Ill.

The Diagnosis and Treatment of Intestinal Amebiasis. Charles F. Craig, South. M. J. **25**:1207 (Dec.) 1932.

The author concludes that the general treatment of amebiasis in those suffering from diarrheal or dysenteric attacks consists in rest in bed and attention to the diet and general physical welfare of the patient. If the dysenteric symptoms are very acute, it is best to withhold all food for two or three days, and if food is given it should consist of barley water, egg albumin, milk with solution of calcium hydroxide and thin broths. When the acute symptoms subside, a semisolid bland diet should be substituted. During convalescence a full diet is generally resumed, but the food should be low in residue. Schlutz, Chicago.

The Precipitation of Diphtheria Toxoid by Metallic Salts. M. L. Smith, J. Path. & Bact. **35**:663, 1932.

Diphtheria toxoid can be precipitated from solution by salts of most metals having insoluble hydroxides, by some phosphates and by various gelatinous precipitates. The toxoid can in most cases be recovered by elution in phosphate solution or solution in sodium tartrate or citrate. Toxoid precipitated by various precipitants and at various hydrion concentrations is from five to fifty times as pure as the original. The yields of specific toxoid are in most cases from 70 to 95 per cent. Evidence is produced that the toxoid is adsorbed onto the gelatinous precipitate of the hydroxide, the phosphates and the various gelatinous precipitates. The washed precipitates are in general better antigens than the original toxoid, the best results being obtained from precipitates of colloidal aluminium hydroxide, zirconyl chloride, calcium phosphate and alum. Combination of acid precipitation and precipitation by metallic salts results in an efficient antigen with a high degree of purity. Author's Summary. [Arch. Path.]

The Complications and Sequelae of the Exanthemata. Laurence Hughes, M. J. Australia **2**:70 (July 16) 1932.

The complications and sequelae of measles and scarlet fever in childhood are discussed. Hughes stresses the importance of chronic bronchitis and fibrosis which so frequently accompany measles and whooping cough in childhood. Pulmonary tuberculosis is not regarded as a common complication of measles. The importance of nephritis, adenitis, otitis media and arthritis as complications of scarlet fever are discussed. Hess notes that during the past four years in London measles has caused eight times as many deaths as scarlet fever and one and a half times as many deaths as diphtheria. Gonce, Madison, Wis.

IMMUNIZATION IN MEASLES BY PLACENTAL BLOOD. J. SALAZAR DE SOUZA, Arch. de méd. d. enf. **35**:633 (Nov.) 1932.

In the belief that the placental blood from a healthy mother gives better assurance of sterility than blood drawn from the arm, the author has used the former for the past four years in the immunization of infants and children against measles, and in the attenuation of this disease when the blood serum could not be used prior to the third day from the expected exanthem.

In this work he had the necessary cooperation of the staff of the maternity wards in the General Hospital at Lisbon, where patients with communicable diseases were excluded, and where proper precautions could be exercised in the collection of blood.

When untreated blood was used, as in 1929, in a dose of 4 cc., injected intramuscularly, 85 per cent of the twenty-seven children under observation were protected. In 1930, of forty-seven patients given injections, there were ten who presented suppuration, a percentage of 78.7 being protected. During the two years following, placental blood was sterilized in an atmosphere of formaldehyde, and of the eighty-two cases studied, success was attained in fifty-seven, or 70 per cent.

AMESSE, Denver.

INTUSSUSCEPTION DURING AN ATTACK OF MEASLES. A. BERAUD and R. PETRIGNANI, Arch. de méd. d. enf. **35**:664 (Nov.) 1932.

A boy of 2½ years sustained a severe attack of enteritis, in the course of which measles developed. Four days after the onset of the eruption, characteristic signs of intussusception appeared; there was a globular mass in the left iliac region with the usual symptoms of shock and stools containing mucus and blood. On account of the accessibility of the invagination, a barium enema under considerable pressure was first tried and checked with the fluoroscope, but this proved ineffective. The child was immediately operated on, and although the operation was followed by bronchopneumonia, recovery was complete, and the patient was discharged on the fifteenth day.

AMESSE, Denver.

ROENTGEN THERAPY IN THE TREATMENT OF WHOOPING COUGH. RADU and ACKERMAN, J. de radiol. et d'électrol. **14**:559 (Oct.) 1930.

The authors observed two cures of whooping cough following roentgen examination of the chest. Later, a larger number of patients have been systematically treated by roentgen therapy with satisfactory results. Two series of irradiations at seven and eight day intervals were applied to one area on the chest anteriorly and one area posteriorly, the central ray being directed toward the fifth or sixth dorsal vertebra. The following dosage was used: 5 Holzknecht units, 3 mm. aluminum filter, from 120 to 130 kilovolts, 4 milliamperes, at a 60 cm. skin target distance. Immediately following the treatment there was, as a rule, a temporary increase in the attacks, lasting for a period of several days. Then the spells gradually grew milder and farther apart, and within from three to four weeks there was complete cure. Five rather unusual cases are briefly described. Irradiation in these was started during the third or fourth week of the disease, after all other therapeutic methods had failed. The conclusion is reached that roentgen therapy forms a valuable therapeutic agent in the treatment of whooping cough. The effect probably is through the intermediation of the sympathetic nervous system.

LEUCUTIA. [AM. J. ROENTGENOL.]

CEPHALIC TETANUS IN A GIRL OF 12 MONTHS. G. BERGHINZ, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 740.

A report is given of a clinic on cephalic tetanus in which a child of 12½ months was demonstrated. The child fell to the ground on November 2, and received an excoriation over the right eyebrow. The wound was treated at home

with boiled water and salt. On November 15, the parents noticed that the child's face was drawn to the left, and they took her to a physician, who dressed the wound, which contained pus.

On November 19, trismus and stiffness of the neck were first noticed, and on the next day treatment with tetanus antitoxin was started. The child had no fever, vomiting, convulsions or pain. During the next seven days, 150,000 units of antitoxin was given. The child was showing improvement. This condition is spoken of as cephalic tetanus of Rose.

HIGGINS, Boston.

PROPHYLACTIC SERUM IN MEASLES. G. SANPAOLESI, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 780.

The relative numbers of deaths in Europe during the past ten years from the three important contagious diseases are: measles, 701; diphtheria, 589; scarlet fever, 470.

The author's data on protection against measles are as follows:

Of 127 patients exposed to measles and treated with serum of persons recently convalescent from measles, 5 had typical and 9 attenuated measles.

Of 26 patients similarly exposed but treated with normal horse serum, 14 had typical and 2 attenuated measles.

Of 10 children who had recently been treated with diphtheria antitoxin, 4 had typical and 6 attenuated measles. Of 17 who had been similarly treated and later had received convalescent serum, only 3 had measles, in each case in the attenuated form.

Of 20 patients treated with serum of persons who had had measles several years previously, only 1 had measles, and this was an attenuated case. Whole citrated blood of convalescent patients protected 27 of 28 patients.

HIGGINS, Boston.

MORPHOLOGICAL CHANGES OF THE BLOOD AND OF THE BONE MARROW IN BRUCELLA INFECTIONS (MALTA FEVER) OF CHILDREN. F. PARADISO, Scritti med. dedicati a Carlo Comba, ediz., Riv. di clin. pediat., 1929, p. 828.

Bone marrow smears from the tibiae of four and blood smears of thirty-five children with Malta fever are reported on.

In 42 per cent of the cases, there was leukopenia, in 33 per cent a normal leukocyte count and in 25 per cent leukocytosis. Medium-sized lymphocytes are the prevailing type of cell, polymorphonuclear neutrophils and monocytes being diminished in number; eosinophils are present in the early, but not in the late or severe, stages of the disease. The blood picture has no relation to prognosis.

Examination of the bone marrow smears of children shows activity of the precursors of both white and red blood cells. This is not the case in adults.

HIGGINS, Boston.

PELVIC INVOLVEMENT FOLLOWING TYPHOID WITH PATHOLOGIC SUBLUXATION. JOSE MARIA MACERA and B. MESSINA, Arch. argent. de pediat. 3:428 (July) 1932.

This rare condition was observed in a child of 14 years following typhoid. There was involvement of the right hip joint followed by considerable limitation of motion, primarily due to a pathologic subluxation and secondarily to inflammatory conditions about the parts. Only one joint was involved. The organism of typhoid could not be demonstrated from any of the material taken from the affected joint. There was extensive osteitis in the neck and head of the femur. The subluxation was reduced, and a cast was applied. The patient continued to improve, and apparently made a complete recovery, although the author does not mention complete restoration of motility in the affected limb.

SCHLUTZ, Chicago.

Septicemia Due to a Bacillus of the Influenza Group. A. Caballero Geisse, Rev. chilena de pediat. **2**:388 (Aug.) 1931.

The condition occurred in an infant 1 year of age and began with otitis media of the left ear. There was early involvement of the left leg, which was held in flexion, and an abscess of the left foot developed. The condition was plainly a septicemia complicated by various metastases.

An organism classified under the influenza group was demonstrated in the blood, spinal fluid and periarticular pus. The antipyogenic vaccine of Bruschettini was tried, without success.

Schlutz, Chicago.

Amebic Dysentery in the Infant. Eliecer Lara, Rev. chilena de pediat. **3**:329 (Aug.) 1932.

This condition occurred in an infant, aged 22 months, who had been breast fed for sixteen months and then given cow's milk and semisolid food. Severe sepsis and extreme dehydration developed, which caused the case to terminate fatally.

Extensive ulcerations with necrotic changes in the intestinal wall were found throughout the middle and third portions of the colon. The etiologic factor was an amebic infection.

Schlutz, Chicago.

Complications of Vaccination, with Special Reference to Encephalitis. J. Baló and F. Lörincz, Jahrb. f. Kinderh. **131**:106 (March) 1931.

The cerebral complications of vaccinia lack uniformity and are probably due to various causes.

Clausen, Rochester, N. Y.

Dysentery in Leipzig. E. Hässler, Jahrb. f. Kinderh. **131**:284 (May) 1931.

During the years from 1926 to 1930, inclusive, positive cultures were obtained from the stools in 235 cases of dysentery in children. Using the classification of Kruse, Hässler identified the types as follows: A, 8; D, 20; E, 180; H, 9; I, 6; unclassified, 12. The E type is distinguished by fermentation of rhamnose. Mortality, in percentage, for the different types was: A, 37.5; D, 30; E, 18; H, 11, and I, 50. An attempt was made to immunize patients in the hospital by intracutaneous injection of vaccine made from selected strains. Of 4,000 children thus treated, 25 in spite of two or more injections acquired dysentery while in the hospital. Patients with severe dysentery did not seem to be helped by transfusion, infusion, injection of dextrose or bacteriophage.

Clausen, Rochester, N. Y.

Salivary Secretion in Mumps. N. R. Schastin, Jahrb. f. Kinderh. **131**:304 (May) 1931.

Diminished secretion in the affected gland is demonstrable by the method of Krasnogorsky. The conditioned secretory reflex disappears for about two weeks.

Clausen, Rochester, N. Y.

Diphtheritic Polyneuritis. Otto Krönig, Jahrb. f. Kinderh. **135**:113 (March) 1932.

On the basis of recent views in the literature and of cases of his own, Krönig believes that diphtheritic polyneuritis begins as a pathologic condition of the nerve roots which extends both toward the periphery and into the cord. He treats the condition by intraspinous injection of from 3,000 to 5,000 units of antitoxin, repeated from two to four times.

Clausen, Rochester, N. Y.

Blood Groups and Scarlet Fever. Hermann Körwer, Jahrb. f. Kinderh. **136**:59 (June) 1932.

The blood group is without influence on the incidence of scarlet fever and on the number or severity of its complications.

Clausen, Rochester, N. Y.

BACILLARY IMMUNITY IN DIPHTHERIA. E. HOEN and L. TSCHERTKOW, Zentralbl. f. Bakt. (Abt. 1) **120**:320, 1931.

The authors gave guinea-pigs subcutaneous injections of cultures of diphtheria bacilli (Park no. 8) which had been washed to remove traces of toxin and killed by 0.5 per cent phenol. Eighteen days later these and normal animals were tested intracutaneously with diphtheria toxin; they reacted alike, which indicated the absence of antitoxin in the vaccinated animals. Similarly, injections with living bacilli killed the vaccinated animals at the same rate as the normal ones. The authors conclude, therefore, that immunity to diphtheria is antitoxic rather than antibacterial.

CANNON, Chicago. [ARCH. PATH.]

ACTIVE IMMUNITY IN THE GUINEA-PIG, HORSE AND MAN WITH TETANUS ANTITOXIN. B. FEIERABEND, Časop. lék. česk. **69**:1457 (Oct. 24) 1930.

Using a sensitive titration method for estimating antitetanus serum which is sensitive to 1/500 UA given intravenously, the author found that the guinea-pig is readily immunized by a single injection of 5 cc., and from two injections, three weeks apart, acquires a thorough immunity which lasts over a year. The horse requires at least three injections of over 10 cc. with an interval of from two to three months between the second and the third injection. In the horse, immunity does not last over a year and the third injection is repeated yearly. In man the permanence of the immunity must be checked in a greater number of cases. In twenty officers immunized with 1, 1.5 and 2 cc. of anatoxin at intervals of three weeks there was a slight elevation in temperature after only two injections; hives occurred in two instances, slight diarrhea in seven and slight infiltration in five cases. Two months after the last injection was given, fifteen had a measurable immunity, that is, three had 1/500 UA, five between 1/500 and 1/50 UA, four between 1/50 and 1/5 UA and three over 1/5 UA. After a year, only eight of them had more than 1/500 UA. A brief review of the literature is included. UA indicates units of antitoxin.

STULIK, Chicago.

A FATAL PLEURAL EMPYEMA FOLLOWING SECONDARY INFECTION WITH DIPHTHERIA BACILLI. Z. VAHALA and M. STOLZ-SUTORIS, Časop. lék. česk. **70**:348 (March 6) 1931.

The author reports the case of a man of thirty-three who had a severe empyema following bronchopneumonia. Tonsillectomy had been done about a month previously. After rib resection a pneumococcic mixed pus drained, and the patient was much improved. Sixteen days after operation, a marked inflammation involved the entire area about the wound, and a dirty discharge and a gray, adherent membrane covered the wound. Viable and virulent diphtheria organisms were recovered from the discharge. The membrane was adherent, and bleeding followed attempts to remove it. In spite of 100,000 units of antitoxin, the patient died. Throat cultures were positive for diphtheria.

In commenting on the review of the literature, the author says that he feels that the authors who regard diphtheritic wound infection as frequent and benign have not been dealing with virulent diphtheria, but with some of the conditions produced by diphtheroid organisms. From the clinical standpoint the local manifestation is difficult to diagnose without bacteriologic study; severe local infection does not overshadow the importance of the general reaction, and the local infection is usually resistant to all therapy either local or general, specific or nonspecific.

STULIK, Chicago.

GROUP IMMUNIZATION OF SCHOOL CHILDREN WITH ANATOXIN OF RAMON. THEODORE VLK, Časop. lék. česk. **70**:557 (April 17) 1931.

About seven hundred children were started on the regimen of three injections, but some obtained only one or two because the parents refused cooperation on

account of slight reactions or the fright of the child. The reactions were a slight elevation of temperature in a few children, a few cases of urticaria, and nausea and vomiting in several instances. The disadvantages of this procedure are that three injections are given at intervals of three weeks and that the associated pain causes an uproar among the children. During the period of observation, diphtheria developed in four unprotected children, and in three who had been given only two injections; two of the three recovered and one died. In none of the children obtaining 0.5, 1 and 1.5 cc. of anatoxin at intervals of three weeks did diphtheria develop during the period of observation which included a mild epidemic in the town. The period of immunity has not been established. The problem of whether the drop in the number of cases may have been due not only to the injections, but also to the fact that the epidemic was ebbing is discussed.

STULIK, Chicago.

DIPHTHERITIC COMPLICATION OF SCARLET FEVER; ETIOLOGY OF SCARLET FEVER RHINITIDES. F. PAVLICA, Časop. lék. česk. **70**:825 (June 5) 1931.

The author noted diphtheritic rhinitis in 20.5 per cent of a series of 219 patients with scarlet fever in the convalescent ward. Other complications were: otitis, in 2.3 per cent; purulent adenoiditis, in 1.8 per cent, and nephritis, in 0.4 per cent. Clinically the tendency of the rhinitis was toward dryness, although at times the condition was sanguinopurulent. Cultures and animal experimentation revealed virulent diphtheria organisms. The Schick test was usually negative. Complication was most common in the third and fourth weeks of convalescence. Following the war, because of the small number of cases, patients with scarlet fever and those with diphtheria were kept in the same pavilion. Since 1925 the increase in the number of cases of diphtheria has been as follows: 1925, 17 cases; 1926, 34 cases; 1927, 91 cases; 1928, 135 cases; 1929, 190 cases, and 1930, 320 cases. After the frequency of the complication of diphtheria was noted, all patients with scarlet fever and those with diphtheria were kept separated.

STULIK, Chicago.

POSTVACCINAL ENCEPHALITIS. HERMAN SIKL, Sborn. lék. **35**:231 (March 7) 1930.

The author reviews the literature and cites statistics on the incidence of encephalitis following vaccination. The case reported is that of a boy, 7 years of age, who became ill on the thirteenth day following vaccination and died five days later. Examination of the brain revealed many microscopic lesions, consisting of perivascular proliferation of glia cells with demyelinization, the affected vessels being essentially veins. The glia cells may contain a certain quantity of lipoid granules, but there is no real softening. The mesenchymal inflammatory reaction of the blood vessels is slight and sometimes entirely lacking; the perivascular lymphatic spaces are often filled with macrophagic cells containing a large quantity of lipoid. Polymorphonuclear leukocytes can be found in the lumen of blood vessels only, their complete absence being demonstrated by the oxydase reaction. Nevertheless the proliferation of glia cells can be considered as an inflammatory reaction. Both the white and the gray substances are affected by the process to the same extent, except for the cortex cerebelli, which was not damaged, and the upper five layers of the cortex cerebri, where only rare foci were found. The severest lesions were found in the thalamus and corpus semiovale. The proliferation of marginal glia described by Turnbull and Schurmann was found only in the pedunculi and, to some extent, also in the bulbus. The process essentially resembles the lesions described up to the present, in cases of postvaccinal encephalitis, though there is a resemblance to postmeasles encephalitis (Wohlwill). One cannot establish the etiologic identity of these conditions on the basis of histologic facts, but it is probable that both conditions are due to the mechanism of action of the same pathogenic agent. The fact that the lesions attain their greatest intensity in places where the tissue fluid leaves the nervous

substance (perivascular and marginal glia) makes one think that the pathogenetic agent is activated only during its passage through the nervous tissue, which is in keeping with the hypothesis of Glanzman. STULIK, Chicago.

FACTS REGARDING PROTECTIVE VACCINATION. W. SZENOJCH, Pediat. polska **2**:310 (May) 1931.

1. The surest method of protection against many diseases is an attack of the disease, which may produce permanent immunity.

2. The best results from vaccination are secured when attenuated bacteria are used, as in smallpox.

3. Vaccination against smallpox does not produce permanent immunity with the same certainty that the disease itself does.

4. The results of research shown by statistics compiled several years ago regarding vaccination against smallpox were not as convincing as those for diphtheria at the present time.

5. Antidiphtheria and antiscarlatina vaccination, under present conditions, will not give the same results as vaccination against smallpox.

6. Vaccination against diphtheria and scarlet fever cannot be made popular, because many children are insensitive to these diseases, and many acquire immunity in a short time.

7. The only value that vaccination can have is its power to give complete protection against a disease.

8. The greatest value of vaccination is that in case the disease occurs it is mild.

9. As vaccination is harmless, research should be undertaken to perfect the methods used. KRUPINSKI, Chicago.

Chronic Infections

JUVENILE TUBERCULOSIS SUSPECTS. ERNST WOLFF, ROBERT S. STONE and FREDERICK EBERSON, Am. Rev. Tuberc. **25**:738 (June) 1932.

In establishing a diagnosis of tuberculous infection in children, the symptoms and physical signs are not conclusive; a history of definite contact is of rather limited value, and certain roentgenologic findings are pathognomonic, that is, hilar calcification, hilar tumor, fibrosis of the lung, calcification of the lung, infiltration of the lung, pleural calcification and calcification of the cervical lymph nodes. The grade of the tuberculin reaction, in terms of the width of the infiltration after the intracutaneous injection of 0.1 cc. of a 1:100 dilution of old tuberculin, is found to be of definite value in diagnosis. It also appears to have a value in deciding the question of the activity of the lesion.

SMITH, Ogden, Utah.

MODERN CASE FINDING IN TUBERCULOSIS. D. S. BRACHMAN, Am. Rev. Tuberc. **26**:89 (July) 1932.

Modern case finding in tuberculosis calls for the testing of all children and adolescents with tuberculin and for the taking of roentgenograms in those cases in which the reactions are positive. When the x-ray picture shows evidence of a pathologic change or is suggestive of such a change, complete physical examination is advisable. The diagnosis is made as the adult type of tuberculosis, the childhood type or the suspect type; in the latter another roentgenogram taken after from four to six months is required. The adult type is the most serious and should be dealt with as the pathologic involvement and general findings require. The childhood type remains a potential adult type, and a child whose condition is in this classification should be examined roentgenologically every six months until he has reached the age of 20 years.

A Study of Tuberculosis Contacts in Families. W. S. Barclay, Am. Rev. Tuberc. **26**:192 (Aug.) 1932.

In this study of 413 contacts in 100 families, demonstrable tuberculosis was found in 21.8 per cent of all contacts, with an incidence of active tuberculosis of 17.2 per cent. The incidence of infection was higher in persons below 5 years and above 15 years of age than in those of the intermediate period. The living conditions of the families investigated were only slightly worse than the average conditions in the community. Intimacy within the home seemed to be of greater importance than lack of food and other conditions depending on economic factors. Of the total number of tuberculin tests (Pirquet) made, 57.2 per cent were positive. Fifty-one per cent of the contacts showed definite or suggestive recent symptoms. Definite or suggestive thoracic symptoms were found in 53 per cent of the contacts of tuberculous children; 84 per cent gave a positive reaction to tuberculin and 88.4 per cent had lesions that were demonstrable roentgenologically.

Smith, Ogden, Utah.

The Incidence of Tuberculous Infection Among School-Children on Five Montana Indian Reservations. H. J. Warner, Am. Rev. Tuberc. **26**:507 (Nov.) 1932.

As determined by the intracutaneous tuberculin test, the incidence of tuberculous infection among the Indian children examined was 62.49 per cent and among white children, 22.84 per cent. In the Indian group there was a steady increase in the incidence of infection with increasing age, which did not obtain in the white group. Indian girls were more frequently infected than boys; the opposite was true among the whites. The incidence of the infection showed a progressive increase in accordance with the degree of Indian blood. The high degree of infection in the Indian group is probably due largely to economic and social causes.

Smith, Ogden, Utah.

Congenital Syphilis. William A. Rosenberg, Illinois M. J. **42**:278 (Oct.) 1932.

The incidence of congenital syphilis is very high. Its first great effect is on fetal and infant mortality. If the infant is born alive, but with signs of syphilis, they are generally so characteristic as to be unmistakable. In many cases the disease is latent at birth, and the infant may appear to be perfectly healthy and symptoms show themselves only later. Cutaneous lesions of late congenital syphilis usually occur after the age of 2 years. Associated with tertiary cutaneous manifestations is involvement of the viscera, bones, teeth, eyes and ears. Prophylactic measures directed against congenital syphilis may be considered from the standpoint of radical eugenics to prevent procreation among syphilitic persons, and active treatment of prospective parents, particularly of the mother during her pregnancy, is advocated. Intramuscular injections of sulpharsphenamine, mercuric chloride or bismuth salicylate, inunctions of mercurial ointment or oral administration of mercury or stovarsol is advocated by various observers for active treatment.

Barbour, Peoria, Ill.

Tularemia from the Ingestion of Insufficiently Cooked Rabbit. Monroe Crawford, J. A. M. A. **99**:1497 (Oct. 29) 1932.

Six members of a Negro family were infected with Bacterium tularense following ingestion of an insufficiently cooked rabbit, which had been found dead. Tularemia developed in one member of the family who had not eaten any of the rabbit, but had helped prepare it. In all instances the path of entrance was through the oral cavity.

Bonar, Salt Lake City.

ACID-FAST BACILLI IN THE BLOOD OF TUBERCULOUS PATIENTS. JOHN F. NORTON AND NORMA H. BROOM, J. Bact. **25**:98 (Jan.) 1933.

The authors made cultures from the blood of 175 tuberculous patients in whom the condition was classified clinically as follows:

Pulmonary:	
Minimal	24
Moderately advanced	70
Advanced	53
Nonpulmonary	13
Unclassified	15

After investigation of various proposed technics, the following was determined on: To 10 cc. of citrated blood, sterile distilled water was added, and the mixture was allowed to stand in the icebox over night in order to obtain complete hemolysis of the red blood cells. In the morning, the tubes were centrifugated for one-half hour at high speed, and the sediment was planted on Petragagni's medium and on a modified Petroff medium. The sediment was divided so that two tubes of each medium were inoculated. The tubes were then sealed with paraffin and incubated. They were examined weekly for ninety days. In no instance was a true tubercle bacillus isolated. From four samples of blood, acid-fast organisms were obtained. These were of a highly chromogenic variety; they grew extremely slowly on egg mediums and did not grow on glycerin agar or plain agar or on Long's synthetic medium. They did not produce tuberculosis when injected into guinea-pigs.

STOESSER, Minneapolis.

TULAREMIA: REPORT OF THREE CASES OCCURRING IN CHILDREN OF THE SAME FAMILY. W. W. WADDELL, JR., and CHALMERS WILLS, J. Pediat. **2**:187 (Feb.) 1933.

Three brothers, aged 11, 8 and 4 years, became ill on the same day with fever and malaise. Each boy had an ulcer on one of his fingers with regional lymph-adenitis. In each case the agglutination test with Bacillus tularense was positive. All three children had handled a dead ground-hog seven days before the onset of their illness, and all three had killed and skinned a small rabbit three days before the acute symptoms appeared.

LEMASTER, Evanston, Ill.

SINUSITIS AND TUBERCULOUS INFECTION. S. PERU, M. J. Australia **2**:350 (Sept. 17) 1932.

The relationship of chronic sinus disease and tonsillar disease to pulmonary tuberculosis is discussed. Removal of foci of infection in the sinuses and tonsils by properly selected operative procedure is suggested as a means of reducing the incidence of invasion of the tubercle bacilli into the body. The author states that 25 per cent of the patients attending his medical clinics suffer from nasal infection. Many tuberculous patients may have the course of their disease favorably affected by the removal of such foci.

GONCE, Madison, Wis.

A CASE OF CARDIOVASCULAR SYPHILIS IN A BOY. H. L. HEIMANN, South African M. J. **6**:377 (June 11) 1932.

The author reports in abbreviated form a case of cardiovascular disease in a 13 year old boy. The cardiovascular changes are thought to be due to congenital syphilis for the following reasons: (1) a history of syphilis; (2) destruction of the soft palate; (3) lack of a history of rheumatism and absence of initial stenosis, and (4) the character of the enlargement of the aorta.

GONCE, Madison, Wis.

LUPUS OF THE SOFT PALATE IN AN INFANT WITH MARKED CERVICAL ADENOPATHY. H. GRENET AND ANDRÉ BLOCH, Bull. Soc. de pédiat. de Paris **30**:22 (Jan. 19) 1932.

A boy, 3½ years old, was admitted to the hospital with a history of a sore throat for about fifteen days. There was a granular, slightly pale area extending over part of the uvula, soft palate and right anterior and posterior pillars and the upper part of the right tonsillar fossa. There was no dysphagia, and the child's general condition was good. The cervical glands were markedly enlarged, especially on the right side. Roentgen examination of the chest showed pulmonary involvement on both sides. The tuberculin test was positive. The father was in a hospital undergoing treatment for pulmonary tuberculosis. The authors have not decided whether the lesion in the throat is primary or secondary. They propose treating the throat by means of diathermy, if the pulmonary lesions do not progress.

BENJAMIN, Montreal, Canada.

EPITROCHLEAR ADENITIS, PROBABLY TUBERCULOUS. BABONNEIX AND RIOM, Bull. Soc. de pédiat. de Paris **30**:24 (Jan. 19) 1932.

A boy, 11 years old, had a swelling about the size of an almond in the epitrochlear region of the right arm. It was partly fluctuating. A tiny amount of thick pinkish fluid was withdrawn. It showed red and white cells but no organisms. The chest showed some calcified glands on roentgen examination. The tuberculin reaction was weakly positive on one occasion but strongly positive two weeks later. It is considered most probable that the adenitis was tuberculous and that the child had hereditary syphilis.

BENJAMIN, Montreal, Canada.

TABETIC SYNDROME: TROPHIC DISTURBANCES. PLANTAR PERFORATING LESIONS. ANALGESIC PSEUDO-WHITLOWS OF THE FINGERS IN A GIRL SIX YEARS OLD. HEREDITARY SYPHILIS. M. WEILL-HALLE AND CLAIRE VOGT, Bull. Soc. de pédiat. de Paris **30**:29 (Jan. 19) 1932.

An interesting neurologic case is reported. By differential diagnosis, syringomyelia, leprosy, Friedreich's ataxia and Dejerine's hypertrophic interstitial neuritis are eliminated, and the case is considered as one of infantile tabes, despite repeatedly negative Wassermann reactions of the blood and spinal fluid. Antisyphilitic treatment was followed by immediate improvement.

BENJAMIN, Montreal, Canada.

THE WORK OF THE SOCIETY FOR THE PRESERVATION OF CHILDREN AGAINST TUBERCULOSIS. P. F. ARMAND-DELILLE, Paris méd. **1**:1 (Jan. 7) 1933.

The author outlines the work of the society in placing children from cities in a country environment. Four thousand infants were placed in this manner, and only twelve cases of tuberculosis developed, with a mortality of three. This is a morbidity of only 0.3 a hundred.

SANFORD, Chicago.

ONE HUNDRED AND TWENTY CASES OF ARTIFICIAL PNEUMOTHORAX IN TUBERCULOUS CHILDREN. P. ARMAND DELILLE, C. HETCHTER and A. MAGRIN, Rev. de la tuberc. **13**:763 (Oct.) 1932.

Artificial pneumothorax, even in young infants, in the opinion of these authors, is without danger or risk, and its beneficial therapeutic effects are incontestable. In older children, unilateral collapse almost always gives good results, even in the presence of cavitation. The indication for its use in the ulcerocaseous form is absolute. In patients with adhesions that preceded or followed insufflation, the practice of oleothorax has almost always given favorable results. In cases in young infants the prognosis is somewhat less favorable. However, if the resistance of the

child enables it to survive until the second year, the prognosis is favorable. If cavities are present, collapse therapy is definitely indicated as the only measure calculated to prevent generalization and to save the infant. In the type of infection termed epituberculosis the indications for pneumothorax are not so imperative, since spontaneous retrogression is possible. When, however, the condition is progressive, as indicated by loss of weight, extension of the shadow and other symptoms, intervention may become necessary. Uniformly favorable results may be expected to follow such treatment.

The authors affirm that in the ulcero-caseous form of tuberculosis in children, pneumothorax is the only therapeutic measure truly efficacious, and that its use is unattended by either danger or inconvenience.

SMITH, Ogden, Utah.

THE VALUE OF SPLENOMEGALY IN THE DIAGNOSIS AND PROGNOSIS OF TUBERCULOSIS IN INFANCY. LEON BERNARD and MAURICE LAMAY, Rev. de la tuberc. **13**:793 (Oct.) 1932.

The authors were able to follow, under exceptionally favorable conditions, 252 children having positive cutaneous reactions to tuberculin. Splenomegaly was present in 31.3 per cent of these children and in only 6.1 per cent in a comparable group of noninfected individuals. The mortality in 79 infected children with splenic enlargement was 36.7 per cent and in 174 tuberculous children with normal spleen, 6.8 per cent. Splenomegaly was present in 70.7 per cent of those dying of the disease. The presence of this sign in children known to be infected warrants a relatively unfavorable prognosis.

SMITH, Ogden, Utah.

IMPORTANCE OF SPINAL FLUID FINDINGS IN THE PATHOLOGY OF LATENT AND CONGENITAL SYPHILIS. V. KAFKA, Dermat. Wchnschr. **95**:1650 (Nov. 12) 1932.

The author made quantitative studies of the albumin in the spinal fluids of patients with latent and congenital syphilis. He determined the globulin, albumin and total albumin content, and believes that an increase in the globulin alone probably indicates a previous syphilitic meningitis. This may occur when all other findings are negative. An increase in the albumin alone also occurs, but there is no satisfactory explanation for this.

L. TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

A CASE OF SYPHILIS CONGENITA TARDA. JOHANNES JOST, Dermat. Wchnschr. **95**:1687 (Nov. 19) 1932.

A gummatous glossitis developed in a youth, aged 19 years. The history excluded the likelihood of acquired syphilis. The Wassermann test and other blood tests were positive. There were no other stigmas of congenital syphilis.

L. TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

JUVENILE TUBERCULOSIS: ITS RELATION TO AGE. I. PEISER, Monatschr. f. Kinderh. **55**:270 (Jan.) 1933.

A study of 4,450 children in welfare stations shows that tuberculosis is particularly to be feared at the beginning and at the end of childhood. It is particularly malignant in infancy, and perhaps for this reason welfare work has been directed almost exclusively to children of this age. The writer urges that more attention be given to the prevention of tuberculosis at the time of puberty.

GERSTLEY, Chicago.

ANOTHER SIGN OF CONGENITAL SYPHILIS. D. N. PLISHKIN, Sovet. vestnik venerol. i dermat., 1932, no. 5, p. 16.

The author has noted among the Buriat population with congenital syphilis a thickening of the medial end of the right clavicle. This is called the "sign of

Gigumenakis," for Gigumenakis described the condition in 1928 among Greeks with congenital syphilis. In left-handed persons, this thickening is seen on the left clavicle. The author has found this sign in 70 per cent of his patients with congenital syphilis, 80 per cent of whom had other evidence of congenital syphilis. Usually there is no pain, although the thickening sometimes reaches large dimensions. In three of his patients who complained of pain at night, antisyphilitic treatment removed the pain, but the osteoperiostitic growth did not diminish in size.

BLOOM, New York. [ARCH. DERMAT. & SYPH.]

Internal Diseases

TUMORS OF THE THYMUS. HARRY M. MARGOLIS, Am. J. Cancer (supp.) **15**:2106, 1931.

Tumors of the thymus gland may originate from the parenchyma (the cells of the reticulum, the small thymic cells or thymic lymphocytes, and the corpuscles of Hassall) and from the stroma (lymphosarcomas, fibrosarcomas, myosarcomas or lipomas), and since the histogenesis of the thymic elements is still *sub judice,* the classification of thymic neoplasms is not possible at present. Margolis considers that the term thymoma for all tumors derived from the parenchyma of the organ is more acceptable than their discrimination into carcinomas and lymphosarcomas.

Tumors included in the group of lymphosarcomas are probably not other than a morphologic variation of a type cell derived from the thymic reticulum. The designation sarcoma should be reserved for tumors derived from elements of the stroma.

The observation of typical corpuscles of Hassall resulting from degeneration of epithelial cells of tumors apparently derived from the thymic reticulum suggests an analogous mode of formation of these thymic corpuscles in the normal thymus. The article is accompanied by very good photomicrographs and by a complete bibliography.

FRIED, Boston. [ARCH. PATH.]

PSEUDOFRACTURES (HUNGER OSTEOPATHY, LATE RICKETS, OSTEOMALACIA): REPORT OF A CASE. L. A. MILKMAN, Am. J. Roentgenol. **24**:29 (July) 1930.

The common site of these spontaneous pseudofractures is about 1 inch (2.5 cm.) below the epiphyseal line of the femur, though any bone may be affected. There is no separation of the parts, although slight injury may produced complete fracture. The lesion starts as a small punctate area which gradually encircles the entire cortex. There is no evidence of curvature or deformity of the bone. The etiology is obscure, but the hypotheses include vitamin deficiency, starvation, parathyroid lesion, rachitis tarda and other deficiency syndromes. The differential diagnosis includes osteopsathyrosis, fragilitas ossium, osteopetrosis, multiple myeloma, malignancy, syphilis, insanity, osteogenesis imperfecta and dystrophia myotonica. There is a bibliography.

STULIK, Chicago.

ANOMALOUS ENLARGEMENT OF THE LIVER AND A DISSECTING HEMATOMA OF THE PHRENIC NERVE. KARL KORNBLUM and GEORGE W. STEVENSON, Am. J. Roentgenol. **24**:38 (July) 1930.

A girl of 16 months was admitted for treatment with a diagnosis of acute otitis media, acute stomatitis, bronchopneumonia with empyema, and diarrhea. The roentgen picture revealed a diffuse mottling of both lungs, with a dense shadow at the right base, which in the lateral view gave a characteristic appearance of an interlobar collection between the right middle and lower lobes. Later roentgen examination revealed a typical paradoxical movement of the right diaphragm, indicating a paralysis of the right phrenic nerve. Treatment had consisted of five transfusions and several subcutaneous injections of physiologic

solution of sodium chloride. Observations at autopsy included multiple puncture wounds in the neck along both sternocleidomastoids, with a small subcutaneous hematoma over the inner end of the clavicle. There were a high right diaphragm to the second space anterior, with no thickening of the muscle, and a much enlarged liver with a right lobe 15 cm. in thickness. Under the pleura on the right of the mediastinum, a liquefying hematoma was seen, extending down the course of the large veins, involving the right phrenic nerve, both by surrounding it and by distending the tissues in which it lay. This hemorrhage had forced its way into the thymus and could be traced up to the sites of the transfusions. This case presented two unusually interesting features. The anomalous enlargement of the liver is probably of such rare occurrence as to be of little clinical importance. The possibility, however, of a paralysis of the diaphragm as a complication in the use of the jugular veins for the purpose of transfusion affords knowledge of distinct clinical value.

STULIK, Chicago.

CASE OF CHRONIC INTERSTITIAL NEPHRITIS WITH HYPERTENSION AND ALBUMINURIC RETINITIS IN A CHILD. L. M. LINDSAY, Canad. M. A. J. **26**:455 (April) 1932.

A girl of 13 years had always been sickly; she had had measles, varicella, pertussis, mumps, diphtheria and enteritis. The tonsils had been removed at 3 years.

The first symptoms of involvement of the kidneys came on in September, 1930. She was brought to the hospital in March, 1931, with the complaint of headache, vomiting, abdominal pain and poor appetite.

The urinalysis showed: a clear, pale urine; specific gravity, 1.007; acid; no sugar; albumin, + +, and a few red blood cells and granular casts. The urea nitrogen of the blood increased from 21 to 204 mg.

The patient died in uremic coma about four weeks after entering the hospital. Postmortem examination showed the typical changes of an interstitial nephritis.

MOORE, Omaha.

FOUR CASES OF OSTEOGENESIS IMPERFECTA IN ONE FAMILY. W. G. TURNER and N. W. MCCLELLAN, Canad. M. A. J. **26**:659 (June) 1932.

A summary is given of four cases of osteogenesis imperfecta occurring in one family. There were six children in the family, four of whom are described in the report. One of the other children a boy, the third child, is apparently healthy in every respect; the other, a girl, the sixth child, has occasional gastro-intestinal upsets and slightly bluish sclerae. There are no deformities from fractures and no history of any.

The family history on both sides is practically irrelevant. A brother of the father had three children, all of whom died shortly after birth and all of them had severe deformities of the hands and feet. The father and mother are blood relatives.

MOORE, Omaha.

NUTRITIONAL ANEMIA IN INFANCY: ITS TREATMENT WITH LIVER EXTRACT AND IRON. JOSEPH GREENGARD, J. Am. Dietet. A. **8**:33 (May) 1932.

Production of simple anemia probably depends on a deficiency of organic and inorganic elements or of a food accessory substance necessary to bring about utilization of these elements. Such deficiency may be due to a lack in the dietary or to failure of storage at birth. Two thirds of the iron store is laid down during the last three months of fetal life. There is five times as much iron in the new-born animal's liver as in the adult liver. There is a rapid decrease to about the age of 4 months, due to absence in the dietary of both iron and specific accessory food substances. Copper as such or as impurities may be a factor.

The age in the groups studied ranged from birth to 1 year. A series of infants was placed on a diet containing iron, a second on liver extract and a third on a combination of liver extract and iron.

The iron salt used was saccharated ferrous carbonate in doses of 1 Gm. three times a day. On this the gain in hemoglobin was not satisfactory until liver extract also was added.

The second group, receiving liver extract, did not gain hemoglobin satisfactorily until iron also was added.

The third group, receiving 1 teaspoonful of liver extract and 1 Gm. of saccharated iron carbonate three times a day, gained an average of 26 per cent of hemoglobin and 1,070,000 red cells.

It was noted that liver extract produced a definite improvement in general nutrition, giving the impression that the active principle in liver concerned in hematopoiesis has a beneficial effect on the tissues of the body and that utilization of foodstuffs is greatly enhanced after liver therapy.

PARKER, Rochester, N. Y.

THE EFFECTIVENESS OF METHENAMINE AS A URINARY ANTISEPTIC AT VARIOUS HYDROGEN ION CONCENTRATIONS. HENRY F. HELMHOLZ, J. Pediat. **1**:73 (July) 1932.

The effectiveness of methenamine is dependent on the splitting off of formaldehyde in an acid medium. The amount of formaldehyde is dependent on the concentration of the methenamine, the acidity of the medium and the time for action. In this series of experiments, plain broth and urine were adjusted to values of p_H varying from 6.5 to 3.5 and inoculated with living cultures of colon bacilli; varying concentrations of methenamine were added and the whole incubated for from two to twenty-four hours, after which plates were poured and the resulting colonies counted.

Even at p_H 4.5 the urine in the control tubes still contained viable organisms after twenty-four hours of exposure at 37 C. (98.6 F.). In contrast, the urine of p_H 4.5 containing 0.05 per cent methenamine was sterile at the end of four hours. With slightly larger concentrations of methenamine, 0.125 per cent, the urine was sterile after four hours at p_H 5.0, but it was not sterile at p_H 5.5, even with 0.5 per cent methenamine after six hours. In all experiments with p_H 6.0 and in all concentrations of methenamine with one exception there were innumerable organisms in the incubated urine after twenty-four hours.

It is evident from the experiments that, if the organisms are to be killed in an interval corresponding to the average stay in the urinary tract (from four to eight hours), the urine must have a p_H below 5.5, preferably as close to p_H 5.0 as possible. The first step in the treatment with methenamine is to render the urine acid to a p_H 5.0 with ammonium chloride. Methyl red is the indicator of choice, because it changes from yellow to deep red when placed in a solution of p_H below 5.5. After the urine shows acidity below p_H 5.5, administration of methenamine is started, and the dose is increased gradually until the urine is sterile or until evidence of irritation of the bladder is seen.

LEMASTER, Evanston, Ill.

ANEURYSM OF EXTERNAL ILIAC ARTERY AND GANGRENE OF LEG AS COMPLICATIONS OF BACTERIAL ENDOCARDITIS. J. B. BILDERBACK, J. Pediat. **1**:82 (July) 1932.

A fatal case of subacute bacterial endocarditis with aneurysm of the left external iliac artery and gangrene of the left leg is reported. There were an embolic thrombus of the left popliteal artery and widespread embolic manifestations causing meningitis, nephritis and infarcts in the spleen. The author explains the aneurysm as probably being the result of endarteritis which in turn had its origin in a septic embolus either in a vas vasorum or lodging on a fatty plaque of the intima.

LEMASTER, Evanston, Ill.

HEMOGLOBINURIA IN CHILDHOOD. MURRAY H. BASS and GEORGE J. DINANDES, M. Clin. North America **15**:1085 (March) 1932.

This condition, rare in childhood, is usually the result of the destruction of large numbers of red blood cells. It may occur during the course of acute infections, after the ingestion of certain poisons and in certain cases of syphilis. It is a rare accompaniment of hemolytic jaundice. A severe form, "blackwater fever," complicates malaria in the tropics. The etiology of the condition was apparently different in each of the four cases reported in this paper. In the first it followed the transfusion of citrated blood, which later was found to have been incorrectly matched. The second case was probably one of Winckel's disease. This case is of special interest from a therapeutic standpoint. Treatment was by exsanguination transfusion. The symptoms rapidly subsided, and the patient was discharged, cured, at the end of two weeks. The third case occurred in a child of 3 years and was characterized by intermittent general convulsive attacks accompanied by hemoglobinuria. The condition was thought to be of syphilic origin, since the child had a 4 plus Wassermann reaction. In the fourth case, a boy of 8 years became acutely ill with high fever and signs of an acute infectious process. Hemoglobinuria developed, and there was a rapid drop in hemoglobin to 32 per cent. His recovery was prompt following a transfusion. The etiology in this case was probably an acute infection accompanied by massive sudden destruction of blood.

SMITH, Ogden, Utah.

COMMON COLDS AMONG CHILDREN. SAMUEL GOLDBERG, M. J. & Rec. **135**:289 (March 16) 1932.

During the winter one of the greatest problems that face the physician is the prevention and treatment of the so-called common cold. Because colds occur more often in cold weather, the impression prevails that it is the cold weather that transmits this ailment. Accordingly the misguided parent excludes every bit of fresh air from the room and then brings the temperature of the room 15 degrees above normal. On the other hand, there is the parent who follows Gandhi's early teaching regardless of the physical stamina of the child. The common cold is as infectious as any of the infectious diseases. Proper diet, proper elimination from the bowels and plenty of sunlight, cod liver oil and viosterol build up a resistance against infections. Children's play and rest must be directed. They do not know by instinct, as do animals, when it is time to rest. A consideration of the prevention of cold is frequently a consideration of the prevention of pneumonia.

WILLIAMSON, New Orleans.

REASONS FOR THE USE OF CARBON DIOXIDE WITH OXYGEN IN THE TREATMENT OF PNEUMONIA. YANDELL HENDERSON, New England J. Med. **206**:151 (Jan. 28) 1932.

The use of oxygen in the treatment of pneumonia is becoming common. The use of carbon dioxide with oxygen is also finding an increasing number of advocates among those who have used it. It appears that many physicians have found that 5 or 7 per cent carbon dioxide (5 per cent carbon dioxide and 95 per cent oxygen, or 7 per cent carbon dioxide and 93 per cent oxygen), which the H-H (Haggard-Henderson) inhalators contain, is effective not only in overcoming cyanosis, but also as a stimulant in the depression resulting from acute pneumonic conditions.

In health the lungs are kept constantly expanded and their airways open. Through these tubes they are the best drained organs in the body. The force that keeps them open is the tonus of the diaphragm and the other muscles of the thorax. Whenever this tonus is lowered, as it is after anesthesia, asphyxia, immersion and, especially after abdominal operations, as well as in elderly and debilitated patients long confined to their beds, the vital capacity of the lungs is greatly diminished. In the unaerated areas mucus accumulates until some of the airways are filled and

closed. The occluded lung or lobe or lobules are soon collapsed, and in such collapsed areas any bacteria that happen to be present find conditions favorable for their growth and activity. It is essentially in this way that all secondary pneumonias develop. The common sequence is lowered muscular tonus, decreased vital capacity, occlusion, atelectasis, pneumonia.

When, on the contrary, respiration is stimulated, as it is in normal muscular activity by an increased production of carbon dioxide in the body, or as it is by inhalation of carbon dioxide, the tonus of all the muscles of the body, and especially those involved in respiration, is increased. The lungs are expanded, occlusion of airways is prevented, and any parts that have already been occluded are reopened. The normal drainage from the lungs through the airways is maintained, or reestablished, and the development of a secondary pneumonia is prevented.

Essentially the same considerations apply to pneumonia of the new-born, which, until recently, has caused death within the first month of life to an average of four of every hundred babies. In nearly all of these patients the infection starts in areas of the lung which have remained in the prenatal state of atelectasis. In maternity hospitals where inhalation of carbon dioxide mixed with either oxygen or air is employed to induce deep breathing, the mortality from this cause has been greatly decreased or altogether eliminated. The same treatment is now being tried as a means of clearing the lungs and controlling the spasms of coughing after pertussis. It appears probable that by this means the frequency of secondary pneumonia, which now often follows pertussis and is responsible for a large part of its mortality, will be considerably diminished.

In the pneumonias originating in influenza and other infections of the nose and throat or in chill and other conditions that bring patients to the medical wards of hospitals, the element of atelectasis is not as yet so fully recognized.

It is a significant fact that no one has yet reported the cure of an experimentally induced pneumonia by means of a vaccine, a serum or an antitoxin. On the other hand, experimental pneumococcic pneumonia has been cured with carbon dioxide.

The author's conclusions are: "The advantages afforded by the use of carbon dioxide, together with oxygen in the inhalation treatment of pneumonia are as follows:

"(1) Deeper breathing is induced, which prevents the development of occlusion and tends to open parts of the lungs already occluded.

"(2) Under inhalation of carbon dioxide, morphine or other narcotic drugs may be used more freely to counteract excitement and restlessness. The stimulus to respiration afforded by carbon dioxide tends to counteract the depression of breathing which such drugs otherwise induce.

"(3) Carbon dioxide in solution becomes carbonic acid and tends to exert a bactericidal action upon the pneumococcus and a resolving action on the pneumonic exudate. These effects are best obtained when inhalation of carbon dioxide is combined with administration of morphine or other narcotic and respiratory depressant drugs. While carbon dioxide tends to lower the p_H of the blood and of the pneumonic exudate, it does not decrease the blood alkali or tend to induce an acidosis, but rather the contrary.

"The tent here shown while suitable for the treatment of pneumonia patients with oxygen is especially designed for their treatment with carbogen, a mixture of carbon dioxide and oxygen."

GENGENBACH, Denver.

ACUTE PNEUMOTHORAX: REPORT OF A CASE IN AN INFANT OF SEVEN MONTHS. HENRY W. HUDSON, JR., New England J. Med. **206**:291 (Feb. 11) 1932.

The case reported is of interest because of its rarity. A white infant of 7½ months was admitted to the hospital because of increasingly severe respiratory distress. At 7:20 p. m., the day before entrance, the infant had suddenly cried out as if in acute pain, and increasing respiratory distress developed, with rapid,

grunting respirations. These symptoms increased during the night, and on admission to the hospital the respirations varied between 70 and 80 per minute. The patient's expression was anxious, and there were slight cyanosis and movement of the alae nasi. The heart and mediastinum were displaced to the left, and the liver was displaced downward so that its inferior border was palpable just above the pelvis. The right side of the chest appeared full, and respiratory movements were limited as compared with the left. On percussion there was a high-pitched, hyperresonant note over the entire right side of the chest. Breath sounds were audible but suppressed, and no râles were heard. The temperature was 99.6 F.; the pulse rate, 160, and the respirations, 78. The red blood cells numbered 4,350,000; the hemoglobin, 60 per cent (Tallqvist); the white blood cells, 31,800, with 77 per cent polymorphonuclear cells. The urine was normal.

Roentgen examination revealed an apparently loculated pneumothorax on the right, with partial collapse of the lung, displacement of the heart, mediastinum and liver, and no evident fluid. Thoracentesis was productive of air under pressure and gave no relief. A catheter was introduced through the ninth interspace in the midscapular line. A large amount of air under pressure escaped, with immediate improvement in the infant's condition. Only a few cubic centimeters of thin, yellow fluid was obtained. The catheter was left in place for water-seal drainage.

GENGENBACH, Denver.

NOTE ON A REMARKABLE BLOOD-SERUM REACTION (WITH FORMALDEHYDE) IN A CHILD. F. PARKES WEBER and E. SCHWARZ, Brit. J. Child. Dis. **29**:117 (April-June) 1932.

A girl, aged 9 years, who had anemia associated with colitic signs, enlargement of the liver and, later, enlargement of the spleen, showed a curious reaction of the blood serum. On the addition of 1 drop of a diluted solution of formaldehyde (36.6 per cent) to 1 cc. of blood serum, the latter became firmly gelatinized. The total albumin content of the serum was 11.4 per cent, of which of 47.4 per cent was globulin and 52.6 per cent serum albumin. Apparently the reaction is not due merely to excess of globulin or of total protein in the blood serum.

A similar reaction of the blood serum is reported to occur in kala-azar. However, the child in the case reported had never been out of England. A diagnostic puncture of the liver is being considered.

LANGMANN, New York.

CONGENITAL PYLORIC STENOSIS. C. MAX PAGE, British M. J. **2**:691 (Oct. 17) 1931.

The author discusses congenital pyloric stenosis along conventional lines, outlining the symptoms and diagnosis, indications for operation, treatment before operation, operating technic, after-treatment, complications and mortality.

ROYSTER, University, Va.

BACTERIAL ENDOCARDITIS IN AN INFANT THIRTEEN DAYS OLD. JOHN D'EWART, Brit. M. J. **2**: 699 (Oct. 17) 1931.

A case of bacterial endocarditis is reported in an infant 13 days of age. The diagnosis was confirmed by autopsy. The primary focus of infection was the septic condition of the cord. This was followed by secondary staphylococcal endocarditis and finally by multiple pulmonary infarction.

ROYSTER, University, Va.

JAUNDICE IN CHILDHOOD. A. C. HAMPSON, Brit. M. J. **2**:932 (Nov. 21) 1931.

The article deals with jaundice as an outstanding symptom, and various causes of jaundice are discussed along conventional lines.

ROYSTER, University, Va.

THE AFTER-CARE OF CONGENITAL PYLORIC STENOSIS. DONALD PATERSON, Brit. M. J. **2**:1176 (Dec. 26) 1931.

The article is introduced by the report of two interesting and unusual cases.

1. A premature child, weighing 2 pounds (907.18 Gm.) at birth and 3 pounds (1,360.78 Gm.) at the age of 7 weeks, had vomited from the time she was born. She was one month premature and died ten days after admission to the hospital with well marked pyloric stenosis.

2. A child, seven weeks premature, vomited from the age of 2 weeks. She died at the age of 8 months, having been admitted to the hospital at the age of 7 months. The condition did not justify operation.

The author reports the mortality among 581 patients with congenital pyloric stenosis admitted to the Hospital for Sick Children during the period from 1917 to 1930, inclusive. He outlines the results, including mortality, operation and complications, stressing alkalosis and postoperative feeding.

ROYSTER, University, Va.

CASE OF MYOSITIS OSSIFICANS PROGRESSIVA. J. BOYD JAMISON, Edinburgh M. J. **39**:393 (June) 1932.

The author was present at the birth of the patient whose case he reports, and has followed her through the twenty-eight years of her life. At birth, the thumbs and great toes were too small, and there was bilateral hallux valgus. However, the patient was well, until the age of 4 years, when a swelling at the level of the second thoracic vertebra was noticed; it was painless, hard and attached firmly to the trapezius muscle. Since then the disease has progressed to the muscles of the shoulders, hips, knees and ankles, always characterized by hard swelling. The woman can progress if placed on her feet, but when leaned against a wall she remains as helpless as a wooden figure. The deeper muscles are soft. The mental condition is bright and happy.

NEFF, Kansas City, Mo.

PROPHYLACTIC VACCINATION IN EPIDEMIC MENINGOCOCCAL MENINGITIS. D. RIDING and N. L. CORKILL, J. Hyg. **32**:258 (April) 1932.

In the northern part of Sudan during the dry, dusty period of the year, outbreaks of meningococcal meningitis occur. An attempt to establish a basal immunity in a portion of the people, with control groups, was made by prophylactic vaccination of the native population, among which there is crowding and poor hygiene.

In this province, with a total of 266,200 people, practically a closed community, there has not been an epidemic of cerebrospinal meningitis for twenty years, the native immunity being very low. With the onset of the epidemic, which lasted for twenty-one weeks with 218 cases reported and 145 deaths, a vaccine (A), which was made from nine strains of type II meningococcus, was given to 10,691 persons. This vaccine contained 2,000,000,000 organisms per cubic centimeter. One dose was given, causing slight fever and discomfort for forty-eight hours. Another group of 10,451 persons was given a stock typhoid-paratyphoid A and B mixture in a similar dose.

The comparative results, studied under strict experimental conditions, indicate that the prophylactic vaccine proved ineffective as a means of combating the disease.

Of the 218 patients, 92 were men, for whom there was a mortality rate of 70.6 per cent and 19 women for whom there was a mortality rate of 79.1 per cent. About the same proportion as to sex applied to children, but the mortality rate was lower, being 57.8 per cent.

JANNEY, Milwaukee.

LYMPHATIC LEUKAEMIA WITH INFILTRATION OF PERIOSTEUM SIMULATING ACUTE RHEUMATISM. F. J. POYNTON and REGINALD LIGHTWOOD, Lancet **1**:1192 (June 4) 1932.

A girl, aged 3 years and 7 months at the time of death was found to be very ill on admission. The first symptoms of leukemia began seven weeks before death and consisted of pains that flitted from joint to joint. On admission to the hospital the patient showed large purpuric spots on the trunk and limbs. The temperature ranged between 99 and 102 F. The blood pressure was 100 systolic and 55 diastolic. The liver was one fingerbreath below the costal margin, and the tip of the spleen was palpable. Examination of the blood showed: red cells, 1,125,000; hemoglobin, 15 per cent; white cells, 4,700, polymorphonuclears, 18 per cent; lymphocytes, 82 per cent; platelets, 10,320; coagulating time, two minutes and forty seconds and bleeding time, over ten minutes.

Roentgenograms of the long bones showed uniform periosteal changes in the femora and humeri. It was thought most probable that these changes had been produced by subperiosteal leukemic infiltration. The child died six days after admission.

At autopsy the more important observations were the following: There was a generalized enlargement and pallor of the lymph nodes, and petechial hemorrhages were noted in the pleura and pericardium. The spleen was firm, slightly pale and not enlarged. Microscopically, there was a slight increase of the trabecular tissue; the lymphocytes were increased and the erythrocytes reduced.

The following striking pathologic changes were seen when the femora and humeri were split open longitudinally: 1. Along the greater length of the bone a layer of the cortex was split from the shaft. 2. At the ends of the diaphysis the marrow was pale and excessively trabeculated. 3. In the marrow cavity there were elongated leukemic deposits.

LANGMANN, New York.

PROGNOSIS IN ACUTE NEPHRITIS IN CHILDHOOD. KENNETH H. TALLERMAN, Lancet **2**:61 (July 9) 1932.

The term "acute glomerular nephritis" is considered a slightly misleading one, since the glomeruli are never found to be solely involved. The cases reported are referred to simply as acute nephritis. Cases of nephrosis are not included. Nephrosis, which is rare, is probably a degenerative condition of the kidney. It may be secondary to a general metabolic disorder; it is probably not a primary renal disease.

There were twenty-nine cases in this series; death occurred in two. Two of the twenty-seven patients who were followed died later; of the rest, only four showed any evidence of persisting renal damage.

"The prognosis of acute nephritis in childhood is good, and does not appear to be necessarily related to the severity of the original attack."

LANGMANN, New York.

THE ORAL TREATMENT OF DIABETES MELLITUS: AN EXPLANATION OF THE SYNTHALIN SYSTEM. T. TODD, W. P. BRINKMAN AND J. R. E. SANSON, Practitioner **128**:531 (May) 1932.

This paper describes the discovery of synthalin, its mode of action and the regimen of treatment, with illustrative cases.

The author concludes that the oral treatment of diabetes mellitus with synthalin is safe, if sensibly administered. It gives as good results as insulin in about 70 per cent of diabetic patients. The system is easy to carry out, needs little supervision and costs about the same as treatment with insulin.

SAPPINGTON, San Francisco.

RENAL RICKETS. HUGH THURSFIELD, Proc. Roy. Soc. Med. **25**:418 (Feb.) 1932.

At age of 1½ years a child was taken to the hospital on account of vomiting and failure to grow. The baby was well nourished for its size and apparently in good health. Double congenital talipes equinovarus was present and also bowing of the legs. The epiphyses at the lower end of the fibulae and femorae showed on roentgen examination changes suggestive of renal rickets. The skin was biscuit-colored. The urine showed albuminuria. The Wassermann reaction was negative. The blood urea was 77 mg. per hundred cubic centimeters; retention of nitrogen was present. The blood calcium and phosphorus were high.

WILLIAMSON, New Orleans.

MIKULICZ'S SYNDROME. A. G. MAITLAND-JONES, Proc. Roy. Soc. Med. **25**:420 (Feb.) 1932.

A girl of 7 years complained that both parotid glands had been swelling for fourteen months unassociated with any constitutional disturbance. On examination the child showed bilateral swelling of the parotid glands which were uniformly soft and painless. No evidence of oral sepsis was present. The Wassermann and Mantoux reactions were negative, as were all the results of other examinations. The author mentioned in his article two other cases occurring in a mother and daughter. The mother had bilateral enlarged lacrimal and submaxillary glands; the daughter, bilateral enlargement of the submaxillary glands.

WILLIAMSON, New Orleans.

CASE SHOWING EFFECT OF NIRVANOL (PHENYLETHYLHYDANTOIN BARBITAL DERIVATIVE) ON SUBACUTE RHEUMATISM. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **25**:717 (March) 1932.

A case showing the effect of phenyl-ethyl-hydantoin was reported in boy aged 7½ years.

WILLIAMSON, New Orleans.

FIBROCYSTIC DISEASE OF THE ULNA. CECIL P. G. WAKELEY, Proc. Roy. Soc. Med. **25**:718 (March) 1932.

A boy, aged 8 years, complained of pain in his left elbow after a fall, and as the elbow appeared to be swollen he was taken to a physician. Hard swelling was palpable at the upper end of the ulna. Movements of the elbow joint were full and free. The skin was not involved. Roentgen examination showed distinct cystic expansion of the upper end of the ulna to the extent of 2 inches (5 cm.). The pathologic report from Nettly Hospital was that the condition was probably a slow-growing fibrosarcoma.

WILLIAMSON, New Orleans.

POLYCYTHÆMIA ANÆMICA SECONDARY TO CONGENITAL CARDIAC SEPTAL DEFECT IN ASSOCIATION WITH AN ANÆMIA-PRODUCING AGENT. F. PARKES WEBER, Proc. Roy. Soc. Med. **25**:789 (April) 1932.

A girl of 4 years was known to have had a congenital defect of the heart since the age of 2 weeks. Since birth she had suffered from periods of cyanosis with lassitude. For the past two years there had been purulent discharge from the left ear at intervals. The tonsils and adenoids were removed two months before this report was made. The heart was enlarged on both sides, and there was a loud systolic murmur over the whole cardiac area, accompanied by a palpable thrill. The blood count showed: hemoglobin, 60 per cent; erythrocytes, 6,400,000, and leukocytes, 19,000. The leukocytosis was due to a condition of the middle ear.

WILLIAMSON, New Orleans.

GAUCHER'S DISEASE. A. ABRAMSON, Proc. Roy. Soc. Med. **25**:789 (April) 1932.

A case of Gaucher's disease was reported in a girl 4¾ years of age.

WILLIAMSON, New Orleans.

CYANOSIS PROBABLY DUE TO DELAY IN EVOLUTION OF THE BLOOD-FORMING MECHANISM. W. M. FELDMAN, Proc. Roy. Soc. Med. **25**:794 (April) 1932.

A case of cyanosis was reported in a boy of 2 months.

WILLIAMSON, New Orleans.

A CASE OF HIRSCHSPRUNG'S DISEASE. JOHN FRASER, Tr. Med.-Chir. Soc. Edinburgh, 1932, p. 19; in Edinburgh M. J., February, 1932.

The diagnosis of the condition in this 12 year old girl was interesting. At the age of 6 a tumor regarded as an osteosarcoma of the sacrum was found in the mid-line of the hypogastric region. Other observations proved that there were associated congenital malformations, an imperfect left ear, a double thumb and a cervical scoliosis. The mass proved to be a megacolon filled with inspissated feces. Left lumbar ganglionectomy produced some favorable results, but not permanent function of the intestine. The author feels that further irrigation of the bowel and tonic treatment will permit better conditions to prevail.

NEFF, Kansas City, Mo.

Nervous Diseases

THE RÔLE OF THE PSYCHIATRIC DEPARTMENT IN RELATION TO THE PEDIATRIC DEPARTMENT IN A GENERAL HOSPITAL. ERIC KENT CLARKE, Am. J. Psychiat. **11**:559 (Nov.) 1931.

The absence or unsatisfactory position of the psychiatric clinic in most general hospitals is deplored by Clarke, who insists that a closer cooperation between the mental hygiene service and the other departments is essential in a progressive institution. The system used at the medical school in Rochester, N. Y., is briefly described. The psychiatric clinic is well organized and the staff is adequate; it is used not only as a consultation service but as a primary clinic for the study and treatment of patients with behavior problems. Attached to the department are two schools, a nursery school for children from 2 to 5 years of age and a training group for children from 8 to 12. In the former school there is active cooperation between pediatricians and psychiatrists. Effort is made to treat the mother also. The older group of children presents more serious problems as a rule, and the program of training is individual, variable and interesting, with much emphasis on manual work. The psychiatric and pediatric services have established a clinic for patients with enuresis and have emphasized the correction of habits due to faulty training and the readjustment of unwholesome emotional situations. In all cases, staff conferences are held in which both departments take an active part. In a discussion of this paper, Robert McGraw warned against excessive enthusiasm on the part of child guidance clinicians, and called attention to the possibility of their work being discredited by too much "ballyhoo" or by inability to produce the results claimed.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

A MENTAL HYGIENE STUDY OF JUVENILE DELINQUENCY. JOHN LEVY, Am. J. Psychiat. **12**:73 (July) 1932.

This paper represents impressions (not, strictly speaking, conclusions) drawn from observations at a small guidance clinic during the last two years. About half of the children at this clinic were delinquents; the other half were used as controls, in spite of the fact that they were all problem children. Levy opens the paper by warning psychiatrists against unscientific procedure as represented by

an insufficient number of case studies or an inadequacy of control groups; this report is itself characterized by both of these defects, a fault which is presumably to be excused because of the author's recognition of it.

Heredity of such qualities as "social stigmas" and "neurotic taints" is reported as being a factor. How much of a factor it is is not stated; the terms are not defined, and case records on which this conclusion is reached are not tabulated or even summarized statistically. The author finds that children of inferior intelligence are more likely to engage in plundering and heterosexual delinquencies, whereas children with superior intelligence commit such relatively complicated offenses as forgery or homosexuality. It is further reported that parents of delinquent children employ different disciplinary measures from parents of nondelinquents. This sweeping statement, important if true, is unsubstantiated by any reported data in this paper. In any event disciplinary irregularities can be found in the delinquent group, ranging from overprotection to neglect. Physical status is also correlated with social misbehavior, the virile boys being the leaders, the effeminate the followers of juvenile gangs. This finding is suspiciously similar to one's a priori conclusions, and it is unfortunate that Levy failed to cite the enumeration of cases by which it was reached. Not only were physical defects found, but mental examinations often gave positive results, the commonest diagnosis being constitutional psychopathic inferiority.

While attaching proper importance to intrapsychic conflict, the author believes that external forces, e. g., bad conditions in the neighborhood, play significant rôles; there is, furthermore, a group of delinquent children whose problems are due to absence of conflict. Of the various personality relationships which break down in these children, relationships to other members of the family are the most important. Second in importance is a distortion in relationships between children themselves. Sex conflicts are also stressed, as in some instances a child falls back on a delinquency such as stealing as an escape from sexual misbehavior. Importance is also attached to cultural conflicts between parents and children.

For purposes of prognostic classification, the author groups offenses as mild and serious according to the depth of their rooting. In the latter class of patients are sexual perverts, those with uninhibited psychopathic tendencies, encephalitic, epileptic, feebleminded, emotionally unstable and neurotic persons and those with sociologic deviations. In the milder group are placed those with cultural deviations, nonresistant and dissatisfied children and those who suffer from sex conflicts apart from constitutional bias. This diagnosis is important for therapeutic purposes. For example, a recreation program would vary with the type of child: The expansive, "bossy" child joins a club where he can be an officer; the sexual invert is invited to take part in artistic activities (dancing, painting, etc.); where cultural conflicts loom large, settlement houses, boy scouts and "Y's" may bridge the gap. The unsatisfied child is assigned to activities where he receives approbation and an outlet for self-expression.

For a therapeutic program, Levy's first recommendation is making a complete change in surroundings, such as may be afforded by a camp, hospital, boarding school or foster-home. If this is impossible, vigorous effort is made to improve the home, both by elevating its material standards and by explaining the mechanisms of the delinquent member's behavior. A recreational regimen is then instituted (as already described). Scholastic conditions are changed if necessary, a trade school, a special tutor, a new teacher or even a new school being prescribed as the case may demand.

The paper is closed by the presentation of a guide to be used by social workers in guidance clinics. It is over 3,600 words in length and is a complete but highly formidable document. The history is divided into ten sections: (1) identifying data, (2) a description of the delinquencies, (3) the developmental history, (4) the child's present make-up, (5) the family history, (6) the history of the siblings, (7) a report of disciplinary methods, (8) the sociologic and environmental background, (9) information about the informant and (10) summary. A briefer outline for an initial psychiatric interview is appended.

The paper is lengthy, and occupies over seventy pages without the presentation of a single statistical summary in support of any of its conclusions.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

FAMILIAL CEREBRAL DIPLEGIA: HEREDODEGENERATIVE DISEASE OF THE NERVOUS SYSTEM. BERNARD S. DENZER, Arch. Pediat. **49**:693 (Oct.) 1932.

Two cases of familial cerebral diplegia are presented. Attention is directed to the rarity of the condition and to the fact that such cases are usually wrongly classified as Little's disease. Features which might serve to differentiate heredodegenerative familial disease from Little's disease are: gradual onset in infancy and progressive course, and association of nystagmus, athetosis, head-shaking and tremor, and consanguinity.

WADDELL, University, Va.

CEREBRAL BIRTH INJURIES; THEIR ORTHOPEDIC CLASSIFICATION AND SUBSEQUENT TREATMENT. WINTHROP M. PHELPS, J. Bone & Joint Surg. **14**:773 (Oct.) 1932.

The classification of cerebral birth injuries has always been made on a neurologic basis. The present classification considers these injuries from the orthopedic angle. Two methods can be used to study the disturbances. Many of the movements are too rapid to be caught by the eye. In these the slow motion picture is of great value.

The five entities or varieties of dyskinesia found in birth injuries or in conditions which are likely to be mistaken for birth injuries are as follows:

1. Spasticity. Voluntary contraction of a flexor group produces a reflex contraction of an extensor group, resulting in impaired motion or no motion at all; that is, voluntary contraction of the flexors of the knee (hamstrings) produces a stretching of the quadriceps, which stimulates contraction of the extensors reflexly.

2. Athetosis. Involuntary, more or less constant contraction of successive muscles without regard to function, in antagonistic or reciprocal groups; that is, involuntary motion of unrelated muscles which produces incoordination as a result of superimposed normal voluntary contraction.

3. Overflow or synkinesia. Involuntary motion results from a voluntary attempt at motion; that is, the facial muscles contract when the patient is writing (sometimes seen in normal persons).

4. Incoordination or ataxia. There is an inability to direct movement in the desired direction; this may be due to the loss of muscle sense, the loss of equilibrium or the interference with muscle balance of peripheral nerve or muscle origin.

5. Tremor. There are fine or coarse, intentional or nonintentional tremors of a rhythmic or of a recurrent nature.

The various types do not usually occur singly; they are usually combined. The relation to attempted voluntary motion must be carefully studied so that the type of treatment can be outlined best.

The presence of any contractures and also the state of muscle balance must be noted.

The treatment consists of: 1. Relaxation. This is of primary importance. Complete relaxation is essential to good results. 2. Treatment of the neck and trunk, with a Thomas collar as a support. Massage and muscle training should be administered. Treatment of extremities can be carried on coincidently. 3. Reciprocal motion; treatment of extremities. The proximal joints must be treated first. Dyskinesia of the shoulder or hip joint negatives the value of a highly trained hand or foot. A year or more is often necessary to produce any improvement in the hip or the shoulder. Five years is the minimum duration of treatment.

In spasticities, relaxation, followed by slow motions, gradually increased so that relaxation is not upset, is of prime importance. Passive stretching in spasticity is always entirely useless. Tenotomies are usually unnecessary, and

tendon lengthening, usually not advisable; tendon or muscle stripping operations are used essentially to give better contractile leverage. Injections of procaine hydrochloride into the nerves may be useful. The injection of alcohol usually destroys function over too long a period. Stoffel operations are valuable to bring about a balance of power, producing greater ease in training.

RYAN, Vancouver, B. C.

NEUROLOGIC CONDITIONS IN INFANTS AND CHILDREN. R. CANNON ELEY, J. Pediat. **1**:614 (Nov.) 1932.

In this critical review, the author discusses the recent contributions to the literature on the following neurologic conditions of infants and children: subdural hematoma in infants, encephalitis (whooping cough, mumps, chickenpox, measles, postvaccinal encephalitis and encephalitis due to lead), epilepsy, encephalography, intracranial tumor, meningitis (influenza, streptococcus, pneumococcus and meningococcus meningitis) and tetany.

LEMASTER, Evanston, Ill.

PSYCHOLOGY AND PSYCHIATRY. BERNARD HART, Ment. Hyg. **16**:177 (April) 1932.

Each science passes through three stages: (1) a period of collection and enumeration of data, (2) a period of description and classification and (3) a stage of interpretation and application. Psychology now finds itself in the second phase. In its endeavor to assist medicine by supplying the physiologic processes of mental disease, psychology appears to have failed. This is a failure, however, not of psychologic methodology, but rather of scientific stubbornness. The effort was made to select from each psychosis its prominent symptom, such as a delusion or hallucination, and to build around that a disease entity. The inadequacy of such a technic cannot be ascribed to psychology, but must be attributed rather to the orthodoxy of psychiatrists who could see no other method except that used in clinical medicine.

The work of Pavlov and Watson is not, in the sense that Hart uses the term, a contribution to psychology. Their refusal to concern themselves with subjective phenomena, especially consciousness, serves to place them beyond the confines of psychologic workers. Lewis Bruce's demand that psychology and psychiatry be divorced is similarly condemned by the author, who brands it as an "attempt to play Hamlet without the Prince of Denmark." These "organic" or "physiologic" approaches are contrasted by Hart (who hastens to assure his readers that this contrast will not lead him into the "either-or" fallacy) with the psychic or "functional" aspect of the problem. The latter method, he agrees, is imperfect, but this should stimulate psychologists to improve rather than to discard their weapons. In any event, psychic concepts should not be rejected if they fail to explain certain phenomena, but only if they contradict them.

Hart reviews briefly the history of psychologic psychiatry, commenting sadly on the failure of the promising attack made by Kraepelin which was to terminate in "an orgy of pigeon-holing." Charcot's proposal that the fundamental phenomena of hysteria might be ideas was a landmark in this history, subsequently developed by Janet and Freud. It was Janet who first used "pure psychology" as an explanation for the neurosis. His willingness to attach this "functional" explanation to such apparently organic signs as anesthesia or paralysis was a significant forward step. It was not until the time of Freud, however, that any one thought of assigning a purpose or a meaning to phenomena in purely psychic terms. His refusal to accept the traditional limitations of psychology was an epoch-making event, for he demonstrated that the manifestations, whether organic or purely subjective, of neuroses and psychoses could be explained adequately and reasonably on purely psychic grounds. In view of the adequacy of this method, Hart sees no reason why the psychologist should court so assiduously the physiologic approach. Mechanism, he insists, is not synonymous with science; indeed the physicist himself is inclining more to abstract ideas and is slowly

abandoning mechanism. He quotes Jeanes: "Knowledge is heading towards a non-mechanical universe, which begins to look a little more like thought and a little less like a machine. Mind, no longer an accidental intruder, is perhaps a creator or governor of matter." With increasing success nature is being interpreted in terms of pure mathematics; yet this is not scientific in the sense that mathematicians formulate their concepts out of their inner consciousness without drawing to any appreciable extent on their experience in the outer world. The psychologist, therefore, should hesitate before accepting the scientific road as the only one which leads to truth.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

THE IMPACT OF CULTURAL FORMS UPON CHILDREN'S BEHAVIOR. JOHN LEVY, Ment. Hyg. **16**:208 (April) 1932.

Not all of the burden of a child's development is to be placed on his emotional or physical adequacy; rather must some of this duty be assigned to society. Children of similar psychic and physical constitution will develop different types of behavior under different social influences. Indeed, one fruitful source of conflict is social instruction—that is, discipline. For example, in children from superior social strata personality problems result from the dual attitude of love and fear toward the parents, while children from inferior economic classes come into conflict with social authority rather than with their own parents. In either case the problems of the child in a civilized community contrast with the cheerful, untroubled maturation of the barbarian in Samoa whose cultural simplicity permits little conflict. The Samoan household consists of thirty or forty persons loosely connected by blood; all of the women assume a maternal rôle toward all of the children; authority is thus so widely dispersed that rebellion is impossible and emotional attachment is innocuous.

The Oedipus complex is an example of the influence of social force rather than an instance of instinctive human response. Thus, in Trobriand Island, society is matrilineal, the family being supported by the mother's brother. Paternity is not understood, and the uncle receives the emotions—love or jealousy—attaching to the father in our culture. In this community, brother and sister are separated and must not show any intimacy; incest between these siblings is the gravest of crimes. Dreams described by the Trobriand Islanders show an interest in precisely this forbidden relationship. There is no taboo on sexual play or overt heterosexual advance with members of another family, and in these islands perversions and frigidity are practically unknown. This may be compared with the sex inhibitions imposed by modern Western culture, resulting (Levy believes) in masturbation, perversion and sexual delinquency. It is probably true that romantic love cannot exist in another type of family and sexual organization, so that it would appear that the emotional and ideal aspects of the relationship blossom as the physical directness of it is hampered.

Not only are the cultural characteristics and the adjustment problems much the result of social forces, but basic temperamental qualities may be viewed as resulting from such conditions. The contemplativeness of the Hindu, the musical inclination of the Negro, the stoicism of the Indian, the passionateness of the Spaniard, the practicalness of the American—are all explicable as responses to simple social forces. Thus, in India, no premium is placed on speed; competition is an inconsequential force. Persistence and patience thus become the desirable Hindu traits.

Even sanity may be considered, to an extent at least, as a cultural concept. Thus in Dobu, every one outside of one's immediate family is considered a witch bent on one's destruction. The generous or tolerant nature is abnormal there, and would be considered insane. On the other hand, a fiercely paranoid attitude is accepted as the proper and right-thinking point of view.

It is well, therefore, to seek for social forces rather than for inherent personal inadequacies as explanation of conflict.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

EPIDEMIOLOGY OF THE 1930 POLIOMYELITIS EPIDEMIC IN KANSAS. EARLE G. BROWN, Pub. Health Rep. **47**:1899 (Sept. 16) 1932.

There were 694 reported cases of poliomyelitis in Kansas in 1930, with 64 deaths. The highest incidence occurred in September and October. In only 25 cases was there a known contact with an acute case of poliomyelitis. In the majority of the patients the paralysis developed on the fourth day after the onset. Only 9.2 per cent did not have paralysis. There was absence of pain in only ten cases during the entire course of the disease. The average cell count on the spinal fluid was 201. Of the 138 cases in which the patients received convalescent serum, 9.4 per cent resulted fatally, as compared to a mortality of 14.3 per cent in the group which did not receive serum.

LEMASTER, Evanston, Ill.

CASE OF MONGOLISM IN INDIA. AMIR CHAND, Brit. J. Child. Dis. **29**:201 (July-Sept.) 1932.

The description does not convince one that this is a case of mongolian idiocy. No mention is made that the hands are short and thick or that the child showed great relaxation of the ligments. Furthermore, the photographs do not demonstrate the typical mongoloid facies.

LANGMANN, New York.

MONGOLIAN IDIOCY. S. ANTONIO, Prat. pediat. **10**:313 (July) 1932.

After reviewing the subject briefly, the author describes a mongolian idiot, aged 6 months. Although both the description and the accompanying illustration suggest a diagnosis of mongolian idiocy, the report would have been more convincing had the author waited to record the further development of his patient.

DOOLEY, Kent, Conn.

MALFORMATION OF THE SKULL IN CASES SHOWING A NASO-ORBITAL ENCEPHALOCELE. H. MUSSGNUG, Frankfurt. Ztschr. f. Path. **42**:238, 1931.

Two cases are reported. In the first instance there was a defect of the skull involving the left frontal bone, and the ethmoid, right nasal and maxillary bones. The left lacrimal bone was entirely missing. In the second instance, the involved bones were the ethmoid, maxillary, nasal and lacrimal. The author believes that both conditions, the malformation of the skull and encephalocele, were the result of one common cause, probably the effect of an outside force directed on the anlage of the skull early in the development of the fetus.

SAPHIR, Chicago. [ARCH. PATH.]

HEREDITARY ATAXIA. S. DAWIDENKOW and N. ZOLOTOWA, Jahrb. f. Psychol. u. Neurol. **44**:377, 1932.

The authors report an atypical case of hereditary ataxia in a woman, aged 44; the illness began at 24, and there was an exacerbation at 33; both of these events followed pregnancy. The disease was characterized by slight remissions. Examination revealed: ptosis, Argyll Robertson pupils, pale optic nerve heads, very slight nystagmus, paresis of the facial and hypoglossal nerves, scanning speech, dysphagia, adiadokokinesis, slight tremor of the hands, cerebellar ataxia in the extremities, cerebellar gait, depressed ankle jerks and progressive intellectual deterioration. The first symptom noted by the patient was ptosis. The patient's three children, though they show slight but definite symptoms of the disease, are not considered abnormal by their relatives. The eldest son, aged 18, has the habit of continuously "raising the eyebrows"; a daughter, aged 17, shows an early but definite dysarthria, sluggish pupils and slight nystagmus; another daughter, aged 8, shows a sluggish pupillary light reflex. The patient's mother, aged 63, has been ill since the age of 30, following an attack of typhus. Her illness is also characterized by frequent remissions. Her pupils are sluggish to light but react normally in accommodation; she has slight horizontal nystagmus, poor convergence, dysphagia, scanning speech,

ataxic gait, dysmetria, slight hypotonia of the extremities and absent patellar and ankle jerks. The patient's maternal grandfather probably also had a mild form of the disease, for he is said to have had dysarthria and dysphagia during the last years of his life. In addition to the direct heredity of the disease through four generations, the patient's maternal aunt had a rudimentary symptom complex of the same disease. This woman's allegedly normal mother, a sister of the patient's maternal grandfather, showed sluggish pupillary light reflexes.

It is noteworthy that, in addition to hereditary ataxia, the family was also burdened with several other hereditary anomalies, such as suicide, depression, oligophrenia (four females and three males), migraine, " nervousness," "irritability," hallux valgus (three generations), and isolated cases of left-handedness and of deaf-mutism.

The authors comment on the variations and mutations of the clinical picture of hereditary ataxia in the various generations in this family, although every case was characterized by the presence of ocular symptoms which may be regarded as basic for this family. These symptoms are disturbances in the pupillary light reflexes, slight nystagmus, poor convergence and ptosis. To a lesser extent, dysphagia was also a basic symptom. It is also interesting that with each successive generation the symptom complex had a tendency to diminish in severity, and one generation escaped the disease.

KESCHNER, New York. [ARCH. NEUROL. & PSYCHIAT.]

MUCK'S EPINEPHRINE PROBE TEST IN DEAF-MUTES. A. KÖRÖSI, Monatschr. f. Ohrenh. **66**:942 (Aug.) 1932.

Körösi found the use of Muck's epinephrine probe test a valuable aid in establishing the etiology of deaf-mutism. Determination of the etiology of deaf-mutism is of interest not only from the standpoint of science, but from that of instruction, as deaf-mutes with remnants of hearing (mostly the congenital deaf-mutes) do not belong in institutions for deaf-mutes but in schools for persons with bradyecoia. The anamnesis is often unreliable in establishing the etiology, because of the unwillingness or inability of parents to give the true facts. The author tried the epinephrine probe test on 116 deaf-mutes. The test subjects were grouped according to Alexander and Fischer's classification of deaf-mutes, which is based on the somatic conditions of the person and his family and the basic etiologic symptoms revealed by anamnesis and clinical examination. The epinephrine probe test was negative in hereditary degenerative disease of the labyrinth. It was negative in patients with individually acquired labyrinthine disease due to intra-uterine trauma or infection. It was also negative in normal persons and in persons of constitutional inferiority who acquired the labyrinthine disturbance after intercurrent disease, either acute or chronic infections. A positive reaction, the white streak sign, was obtained in normal patients or patients of constitutional inferiority in whom labyrinthine disease appeared following trauma or meningitis. The results agree with the author's anticipations in all but three cases.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

A CASE OF APLASIA OF THE CEREBELLUM. N. K. LYSSENKOW, Virchows Arch. f. path. Anat. **280**:611, 1931.

Because of the rarity of cerebellar aplasia in adults this gross and microscopic study of the brain is presented, although the clinical history and a protocol of the necropsy could not be found. It is known only that the specimen was from a man who reached the age of 25 years, that he was said to have been psychically normal, and that he had never walked. The vermis of the cerebellum and all its structures were absent. The lateral lobes were much smaller than is normal. They revealed the normal topography, but all the structural elements were quantitatively greatly reduced. The nuclei and tracts of the brain stem that have no direct connection with the cerebellum were normal.

SCHULTZ, Chicago. [ARCH. PATH.]

IMPRESSIONS AND OBSERVATIONS RECEIVED DURING THIS YEAR'S EPIDEMIC OF POLIOMYELITIS IN FINLAND. ELIS LOVEGREN, Acta psychiat. et neurol. **6**:327, 1931.

The author presents a brief study of the general course of the epidemic of poliomyelitis in Finland. His most interesting observation is that in one area the disease seemed to be spread largely by contact, but in another district its spread seemed to follow the course of the rivers. A similar spread was not observed in connection with railroads or other means of communication unless they lay along streams. He raises the question as to whether some cases of poliomyelitis are not water-borne. PEARSON, Philadelphia. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Eye

REGARDING A FAMILY IN WHICH NEURO-RETINAL DISEASE OF UNUSUAL KIND OCCURRED ONLY IN MALES. E. THOMAS, Brit. J. Ophth. **16**:681 (Nov.) 1932.

The mother of this family had eight living children, four boys and four girls, and she had had two mishaps. All the surviving children were born in abnormal presentation, and in each case there was rather severe postpartum hemorrhage.

The four girls were reported to have normal sight. The four boys had a peculiar macular condition with varying degrees of disease of the optic nerve. In one case it eventually led to retinal detachment in both eyes. There was no mental defect in any of the cases. The characteristic macular lesions were radial streaks which started from a circular foveal area around which were a few dots of the same color as the streaks. The latter could be traced over an area nearly equal to that of the disk, appeared faintly yellow or yellowish gray, and suggested a definite tissue.

The visual field showed a central scotoma for red, green and blue up to an object of about 2 mm. Central vision varied from 1/60 to 6.12.

ZENTMAYER, Philadelphia. [ARCH. OPHTH.]

CONCERNING LACRIMAL CYSTIC DIVERTICULI. MICHAIL, Arch. d'opht. **49**:384 (June) 1932.

The author reports three cases of lacrimal cystic diverticuli. Two of the cases were congenital and one was traumatic in origin. The condition is rare, but has been recognized for many years. Most of these diverticuli have been described as having a prelacrimal location, as in the third case reported by the author. In the first two cases the diverticuli were laterolacrimal in situation, which is exceptional. They may have a congenital origin or be the result of an inflammatory process. MARLOW, Syracuse, N. Y. [ARCH. OPTH.]

NEURO-EPITHELIOMA OF THE RETINA AND CHIASM IN A CHILD AGED FIVE. CL. VINCENT and L. STUHL, Bull. et mém. Soc. de radiol. méd. de France **18**: 296 (July) 1930.

A case of neuro-epithelioma of the chiasm which spread to the retina of the right, and later to that of the left, eye and in which roentgen therapy led to remarkable temporary improvement is described in detail. The good response to irradiation is explained by the fact that the tumor was very cellular and the cells very poorly differentiated. LEUCUTIA. [AM. J. ROENTGENOL.]

THE USE OF SOUNDS IN THE TREATMENT OF DACROCYSTITIS OF THE NEWLY BORN. H. MUJICA and J. VERDAGUER, Arch. d. hosp. de niños **3**:29 (March) 1932.

The use of the sound in the lacrimal ducts is without danger in the dacryocystitis of the newly born. Rapid cure can be effected with its use. Usually only

one treatment is necessary. The author believes that less trauma is produced by this method than by other procedures, such as lavage or massage.

SCHLUTZ, Chicago.

ORBITAL PHLEGMON FROM OSTEOMYELITIS OF THE MAXILLA IN INFANTS. J. KUBIK, Med. Klin. **28**:1097 (Aug. 5) 1932.

The rarity of the condition prompted Kubik to report two cases. A 3 month old infant had a furuncle on the forehead. Three days after it had healed there was a sudden rise in temperature with swelling of the entire right side of the face. The eye was turned down and out, and an incision through the periosteum above and nasally revealed no pus. A day later pus of a streptococcic nature appeared at the opening. The sinuses and nasal passages were clear. Later pus began to discharge from the nose and mouth, and osteomyelitis was diagnosed from a swelling of the bony palate. Roentgenograms showed a sequestration of the maxillary orbit, which was removed, with excellent recovery. During the period of congestion, the veins of the fundus were greatly swollen. The other case was in a 6 week old infant with acute coryza and swelling of the lower left lid. The entire left half of the face was subsequently involved. A mucopurulent discharge came from the nose, and later a small fistula was noted, extending into the gum area of the upper jaw. Staphylococci were found in the discharge from an incision in the lower lid. Subsequently an incision was made in the buccal mucosa with excellent drainage. The bulb returned to normal. Kubik suggests that the condition may be due to an undermining of the orbital periosteum or to a collateral edema of the orbit in which the sinuses play a part. Also a type of Quincke's edema of the orbital fat may predispose to the condition. (Bibliography.)

MAYER, Chicago. [ARCH. OPHTH.]

Diseases of the Ear, Nose and Throat

THE HANDICAP OF CLEFT-PALATE SPEECH. DOROTHY M. WOLDSTAD, Ment. Hyg. **16**:281 (April) 1932.

An unrelieved cleft palate takes a human being out of contact with his own world. Filled with a sense of his inability to meet the social situation, he has feelings of inferiority and insecurity. This is an unnecessary tragedy; surgical skill is fully equal to the task of correcting the deformity, and pedagogy is entirely able to retrain the patient. The intelligence of children with cleft palate is within the normal range of intelligence quotients, and offers no obstacle to speech training. The author suggests that every obstetrician should examine the mouth of each child he delivers; that babies who present this defect should be referred to the plastic surgeon within a month after birth. Correction at this early stage is surgically more simple than a later operation, and it has the additional advantage of saving the child from the emotional hazard of realizing that he has abnormal speech. Speech training must supplement surgical correction in older children. One of the major aims of this is to teach the child to project the air stream out of the mouth instead of through the nose; he should be taught resonance and tone quality. An effort should be made to qualify him in some other field, athletics or music, for example, so that he may have reason to feel superior as a balance to any feeling of inadequacy that his defective speech may produce.

DAVIDSON, Newark, N. J. [ARCH. NEUROL. & PSYCHIAT.]

NASAL INSTILLATIONS IN INFANCY (FATAL MISTOL INTOXICATION). HERMANN BRÜNING, Arch. f. Kinderh. **93**:102 (April 10) 1931.

Several instances are cited from the literature in which dangerous and alarming results followed the use of camphor and menthol in nose drops in infancy. The author reports the case of a 6½ month old infant who after receiving mistol by nasal instillation for nine weeks showed signs of chronic poisoning and finally died.

If nose drops are used in infants it is advisable to use only indifferent fluids, such as plain oil, which can do no harm. If drugs are incorporated into the nasal medication, it is advisable to specify the exact dose and the length of time administration should be continued. LEMASTER, Evanston, Ill.

A POLYP OF THE EDGE OF THE CHOANAE IN A SMALL CHILD. KARL RUPILIUS, Arch. f. Kinderh. **94**:209 (Sept. 11) 1931.

A 3 year old boy was brought to the clinic because of moderate difficulty in respiration. Breathing was easier when the mouth was held open. Examination showed a bluish-red pedunculated tumor the size of a chestnut hanging from the nasopharynx into the throat. After a few days the tumor suddenly disappeared. Posterior rhinoscopy revealed only a small, fibrin-covered spot on the vomer. Apparently the pedicle broke and the tumor was swallowed. Rupilius suggests that this was probably a polyp of the rim of the choanae which pathologically lay midway between a fibrous and a mucous polyp. LEMASTER, Evanston, Ill.

RIGIDITY OF NECK FOLLOWING ADENOTOMY. K. BERNFELD, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **132**:293 (Sept. 21) 1932.

Bernfeld says that rigidity of the neck after adenotomy recently reported by Schaeffer as a rare complication is not so rare as the latter supposes. The author reports two cases. In both of them, as in Schaeffer's, there was no significant demonstrable glandular swelling. As malformation of the epipharynx existed in both cases, Bernfield thinks that an injury of the deeper muscles incurred during intervention in the constricted nasopharynx resulted in myositis and consecutive rigidity of the neck. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

SO-CALLED PERSISTENT CARTILAGINOUS FOCI IN THE REGION OF THE BONY LABYRINTHINE CAPSULE. F. ALTMANN, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **132**:297 (Sept. 21) 1932.

Altmann reports the postmortem finding of an island of cartilage in the upper wall of the internal acoustic meatus in a child aged 2 days, with microtia and congenital atresia of the external auditory meatus on the left side. The island of cartilage was 1.5 mm. in diameter and nearly spherical. It was rich in cellular elements. It was sharply defined from the adjacent bone tissue by a perichondrium-like covering of connective tissue. According to Bast, five ossification centers are involved in the development of the bony internal acoustic meatus, all of which are fused in the 19½ week old embryo. Normally there are no cartilage rests in the superior wall of the acoustic meatus after this period. However, Altmann thinks it possible to attribute the island of cartilage to a cartilage rest which is usually present only a short time and rapidly disappears. Analogously in the course of endochondral ossification of the long bones, islands of cartilage are sometimes excluded during the fetal period or later by injurious influences and may persist while the remainder of the cartilage ossifies. They constitute simple chorista or may proliferate and give rise to tumors. Whether the case reported concerns such a cartilage rest remains unanswered, but in Altmann's opinion this is at least histologically possible. He reports two other cases which show that a retardation of ossification in the fusion zone of Bast's ossification centers may occur under certain circumstances and a certain section of cartilage accordingly be preserved longer. EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

ABSORPTION OF FOREIGN MATTER IN TONSILS: TONSILS AND COLLOIDAL SILVER. G. KELEMEN and A. HASSKÓ, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **132**:326 (Sept. 21) 1932.

Kelemen and Hasskó's study of the absorption of colloidal silver in the tonsils constitutes the third series of experiments in an investigation of the absorption of

foreign matter in the tonsils. Reports on the first and second series of experiments dealing with the absorption of arsphenamine and colloidal gold, respectively, appeared in the *Archiv für Ohren-, Nasen- und Kehlkopfheilkunde* (**130**:222 [May 23] 1932) and was abstracted in the *Archives of Otolaryngology* (**16**:587, 1932). In the present series, the authors experimented with collargol and electrocollargol on human beings and rabbits. With one exception, no silver could be histologically demonstrated within the tonsillar tissue after application of collargol to the surface of human tonsils; neither could silver be demonstrated in the tonsils after intravenous injections of customary doses of another colloidal silver preparation. Collargol and electrocollargol injected intravenously into rabbits in tolerated doses did not reach the tonsils; only when lethal doses were injected could traces of silver in the tonsils be demonstrated. With injection of collargol after elimination of the reticulo-endothelium of the spleen and liver by colloidal copper (amounts up to the lethal dose), the tonsils also remained free from silver even when conditions for phagocytosis were improved by gelatin. Likewise, silver injected into animals after splenectomy and blockade of the liver by copper, and silver injected into a human being after splenectomy, could not be demonstrated in the tonsils of the experimental subjects. The authors conclude that the tonsil does not possess any elements capable of absorbing significant amounts of silver. Even in severe generalized argyrosis there is no significant absorption of silver in the tonsils as there is in the tissue of the surrounding organs.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

HEREDITARY DISPOSITION TO OTITIS MEDIA. O. BESELIN, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **132**:335 (Sept. 21) 1932.

Beselin presents three genealogical tables to illustrate the importance of hereditary disposition in the occurrence of otitis media. In his opinion, the theories which attribute to the local hereditary constitution of the mucosa a rôle in the pathogenesis of otitis media appear well founded. He thinks that the genealogical tables show the indications for prognosis and therapy of otitis media which a careful family anamnesis may contribute.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

Diseases of the Skin

A CASE OF YAWS. M. D. ROJAS, United Fruit Co., Med. Dept., 20th Ann. Rep., 1931, p. 199.

A case of yaws in a girl aged 8 years, living in Panama, is reported. Two other children in the same family had previously had yaws. For five months the girl had had papules and tubercles on the face, neck, legs and perineal region. Dark-field examination of the serum from the papules revealed Treponema pertenue. Complete recovery followed four intramuscular injections of sulpharsphenamine. The author states that the virus of yaws is probably transmitted easily by simple contact in the native children, who go barefooted and naked, and who live in insanitary conditions.

LEMASTER, Evanston, Ill.

FOLLICULITIS ULERYTHEMATOSA RETICULATA. N. BURGESS, Brit. J. Dermat. **44**:357 (July) 1932.

A case of folliculitis ulerythematosa reticulata is described in a girl, aged 14, who presented a symmetrical, pitlike, atrophic, reticulated eruption of slow evolution on both cheeks. No milium bodies were present, and only three comedones were found on the face. The affected areas on the cheeks appeared to be erythematous, and on close examination this was seen to be due to fine telangiectasia. The literature on this disease is reviewed, together with a discussion of the classification of the various reported cases and their exact position in this group. Burgess

states that it would appear from a study of the recorded cases of this condition that one may conclude that folliculitis ulerythematosa reticulata is a follicular dystrophy, probably of congenital origin, related to the other chronic follicular disorders and unrelated to formation of comedones. A clinical photograph and a photomicrograph accompany the article.

WIEN, Chicago. [ARCH. DERMAT & SYPH.]

CONGENITAL ICHTHYOSIFORM EPIDERMOLYSIS. S. LAPIERE, Ann. de dermat. et syph. **3**:401 (May) 1932.

Two cases of congenital icthyosiform erythroderma, one of the typical dry form and the other of a bullous variety, are reported and discussed in detail, with special emphasis on the histology. The whole subject of the congenital icthyotic group of dermatoses, in which there has been so much confusion in nomenclature, is critically reviewed in the light of the two cases reported.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

ACHROMIC (OR INVERSÉ) PITYRIASIS VERSICOLOR. M. E. COHEN-HADRIA, Bull. Soc. franç. de dermat. et syph. **39**:774 (June) 1932.

A young girl who had had considerable exposure to the sun in a bathing suit exhibited a typical pityriasis versicolor on the flanks and lumbar region, but "achromic" lesions on the exposed parts — the neck and the upper part of the back. Instead of the classic brownish plaques on a white background, the lesions appeared as whitish spots on a hyperpigmented background. The author has seen several such cases, and proposes for them the term pityriasis versicolor inversé.

GANDY, Houston, Texas. [ARCH. DERMAT. & SYPH.]

ECZEMA IN AN INFANT, EMPYEMA, IMMUNO-TRANSFUSION, GAVAGE, CURE. M. WEILL-HALLÉ, KOANG and AUBERT, Bull. Soc. de pédiat. de Paris **30**:408 (June 21) 1932.

A boy, 2½ months old, was admitted because of eczema. His stay in the hospital was a protracted one. A staphylococcic empyema developed. The mother was given repeated injections of a vaccine made from the organism removed from the infant's chest, and on the days following these injections, 10 cc. of her blood was drawn and injected into the infant. The infant lost a great deal of weight and had marked anorexia, Gavage of his feedings was resorted to, and he improved decidedly. Repeated aspiration of the chest was done, and after a considerable period the child was cured.

BENJAMIN, Montreal, Canada.

ERYTHEMA NODOSUM AND THE TUBERCULIN REACTION. DENES VON MORITZ, Arch. f. Kinderh. **93**:286 (June 16) 1931.

In ten cases of erythema nodosum about a week after the disappearance of fever and nodules, 0.1 mg. of old tuberculin was injected intradermally. A strongly positive reaction resulted in all patients, and in four of them a recurrence of the erythematous nodules followed. Several other experiments are cited in support of the view that the lesions of erythema nodosum are due to a sensitivity to tuberculin.

LEMASTER, Evanston, Ill.

PALMAR AND PLANTAR KERATOMA IN COMBINATION WITH OTHER DEGENERATIVE SIGNS. GERTRUDE PALM, Arch. f. Kinderh. **93**:307 (June 16) 1931.

An 8 year old boy came under medical observation because of extreme thickening and desquamation of the skin of the palms and soles. At the site of desquamating patches of thickened epidermis the underlying skin was red and covered with abundant sweat of foul odor. The same condition had been present

in four generations of the boy's family. A high arched palate also occurred in all members of the family exhibiting the hyperkeratosis. The condition is considered to be definitely inherited through the germ plasm and not affected by sex. Treatment is symptomatic.

LEMASTER, Evanston, Ill.

FEER'S DISEASE. M. FELLNER, Dermat. Wchnschr. **95**:1541 (Oct. 22) 1932.

A typical case of Feer's disease (juvenile acrodynia) is described in a 1½ year old boy. The only unusual feature was the presence of an enlarged liver. The condition cleared up under treatment with injections of liver extract, and the author believes that dysfunction of the liver may play a part in other cases, in spite of the absence of hepatic symptoms.

TAUSSIG, San Francisco. [ARCH. DERMAT. & SYPH.]

ON THE DEMONSTRATION OF HERPES AND VACCINIA VIRUS BY MEANS OF CORNEAL INOCULATION. H. GASTEIGER and V. NIEDERWIESER, Jahrb. f. Kinderh. **137**:212 (Nov.) 1932.

This article is a polemic against Herzberg's opinions (*Jahrb. f. Kinderh.* **136**: 365, 1932).

CLAUSEN, Rochester, N. Y.

THE ETIOLOGY OF ERYTHEMA NODOSUM. O. KREN, Wien. klin. Wchnschr. **44**:743 (June 5) 1931.

Erythema nodosum is not an infection *sui generis*, but a form of reaction to various acute and chronic infections, to bacterial and fungous invasions of the blood stream and even to chemical substances. The logical consequence of this is that in every case of erythema nodosum the cause of the symptoms should be ascertained in order to choose the correct therapy. The following causative factors are enumerated in the order of their importance: tuberculosis, syphilis, fungi, Trichophyton, lymphogranuloma inguinale and sepsis. The disease often follows angina, for such patients react promptly to vaccine obtained from angina smears, but not to preparations of salicylates or formaldehyde.

ABT, Chicago.

A NEW METHOD FOR EXTERMINATION OF HEAD LICE. L. V. WIKULLIL, Wien. klin. Wchnschr. **45**:175 (Feb. 5) 1932.

A new preparation named *"Lausin"* has been tried out on three hundred pediculous children in convalescent homes with excellent results. It consists of 1 Gm. of yellow mercuric oxide in 100 Gm. of agar-agar. The mixture is shaken well before use and is left on for twenty-four hours. It is odorless, nonirritant and easy to apply.

ABT, Chicago.

DIETETIC TREATMENT OF CONSTITUTIONAL INFANTILE ECZEMA AND OF STROPHULUS INFANTUM. E. URBACH, Wien. klin. Wchnschr. **45**:496 (April 15) 1932.

The problem of infantile eczema is very complicated and far from solution. Opinions of pediatricians in Germany and abroad as to the treatment are widely different and often contradictory. The author suggests that besides a local treatment, an etiologically based, dietetic therapy is highly important.

He divides infants into four groups: (*a*) In overfed infants the quantity of food is regulated in such a way that the weight increases only slowly. This and the local treatment remove most of the eczema. (*b*) Atrophic or dystrophic children should be brought back to normal weight. (*c*) In the exudative type, the hydrolabile body consistency is brought back to normal on a salt-free and fat-free diet. An intracutaneous desensitization should be undertaken when the cutaneous test shows an alimentary hypersensitivity. (*d*) Eutropic children with

eczematous conditions of the skin are treated by changing the intestinal flora, which causes changes in the excretion of acid.

Strophulus infantum in infants and small children is almost always of a nutritive allergic nature. When the specific cause is discovered, the therapy by desensitization or a specific propeptone therapy should be instituted.

ABT, Chicago.

PATHOGENESIS OF ALOPECIA AREATA. VLASTA ŘIHOVÁ, Česká dermat. **13**:96 and 107, 1932.

The author discusses the parasitic, trophoneurotic, reflex and endocrine theories, but favors the view that alopecia areata is the symptom of a systemic disease, namely, a disturbance of internal secretions. The first part of the paper deals with alopecia areata caused by hypothyroidism and hyperthyroidism, by ovarian disturbances of puberty and menopause and by an enlarged hypophysis, and the author discusses syphilitic alopecia, which is considered by many to be identical pathogenically with alopecia areata.

The second part of the paper is devoted to a clinical, experimental and histologic study of thallium alopecia and its relation to alopecia areata. Clinically, the picture of thallium alopecia is identical with that of alopecia areata caused by hypothyroidism. In the described case of thallium poisoning (rat poison taken with suicidal intent), the patient happened to take exactly the epilating dose. Besides a total loss of hair, she showed a positive Hertogh sign, decreased basal metabolism and leukonychia striata involving all the finger-nails. Ovarian disturbance was evidenced by intermenstrual flow. Results of general examination pointed overwhelmingly to a disturbance of the thyroid gland.

By experiments on rats, the author brought out the fact that the diet has a great influence on the action of thallium. A diet rich in casein and vitamin A delays and decreases the epilating effect of thallium. The diet may be one of the exogenous factors influencing thyroid hormone, increasing or decreasing its peripheral effect.

Histologic study brought out the following facts: Thallium has a definite influence on the vitality of epidermal cells. The cells of the hair bulbs are the most sensitive; those of the nail matrix and skin are less so. Thallium hastens the normal shedding of hair. Only in small repeated doses does it lead to atrophy and disappearance of the hair follicles. The author found no degenerative changes in the first stage of hair regression as described by Truffi. Forty-one photomicrographs illustrate this part of the paper. The author concludes that thallium causes alopecia indirectly through its action on the endocrine system. Thallium alopecia is, therefore, not only clinically but also pathogenically closely related to alopecia areata and is regarded by the author as a systemic disease.

SPINKA, Texarkana, Texas. [ARCH. DERMAT. & SYPH.]

Surgery and Orthopedics

A STUDY OF THE PREDISPOSING CAUSES OF BREAST ABSCESS. FRED B. SMITH, Am. J. Obst. & Gynec. **24**:123 (July) 1932.

Several definite statements may be made about abscess of the breast. It is a condition fairly common in a private obstetric practice and is a disease of the primipara and of the blonde. It is two and one-half times as common in fall and winter as in spring and summer. The average abscess occurs during the infant's sixth week, the baby being overweight. It is more common among the well-to-do, and it does not depend on deformities of the nipple. Foci of infection and trauma seem to play a part. There is some evidence that the infection is carried to the breast by the blood stream.

ZIEGLER, Minneapolis.

MASSIVE UNATTACHED RETROPERITONEAL TUMORS. G. H. HANSMANN and J. W. BUDD, Am. J. Path. **7**:631 (Nov.) 1931.

Seventeen retroperitoneal tumors similar to those which occur in the kidney but not attached to the adult urogenital organs are reported. It is suggested that these tumors have the same origin as those which occur in the kidney, and that they probably arise from remnants of the urogenital apparatus.

MOORE, Charlotte, N. C.

LUMBOSACRAL TERATOMA ASSOCIATED WITH SPINA BIFIDA OCCULTA. REPORT OF A CASE WITH REVIEW OF THE LITERATURE. PAUL C. BUCY and H. E. HAYMOND, Am. J. Path. **8**:339 (May) 1932.

A case of teratoma in the lumbosacral region in a 15 month old Mexican girl is reported. This condition is always associated with spina bifida. The tumor in this case contained epithelium similar to respiratory epithelium, smooth muscle, connective tissue, myelinated nerve fibers, a Vater-pacinian corpuscle, a ganglion with typical dorsal root and lymphoid tissue. The author concludes that the teratomas are undeveloped twins, owing to division of the primitive streak during the first four weeks of embryonic life.

MOORE, Charlotte, N. C.

MALIGNANT TUMORS OF THE KIDNEY IN INFANCY AND CHILDHOOD. CHARLES G. MIXTER, Ann. Surg. **96**:1017 (Dec.) 1932.

During the past twenty-one years, in 22,000 admissions to the surgical wards of the Childrens Hospital in Boston, 41 instances of renal neoplasm have been recorded. Renal malignant growths occur in childhood at any age, irrespective of sex. Most of them are seen in the first five years of life. In childhood symptoms are generally absent at first. As the tumor grows the child becomes irritable and evidences abdominal discomfort, but pain is rare. Secondary anemia is usually present, and in the terminal stages there are dilatation of the superficial abdominal veins and rapid wasting. Metastasis usually takes place by way of the blood stream and implicates the lungs, liver and rarely the opposite kidney.

The diagnosis is usually easy. The tumor is usually solid, not tender and smooth or somewhat nodular. Pyelography is usually not necessary for the establishment of the diagnosis. After evidence of metastasis is ruled out, nephrectomy is advocated.

BANTIN, Omaha.

CALCIUM AND PHOSPHORUS OF SALIVA IN RELATION TO DENTAL CARIES. REBECCA B. HUBBELL and RUSSELL W. BUNTING, J. Nutrition **5**:599 (Nov.) 1932.

Saliva of school children from 7 to 16 years of age was studied, with that of control groups. The experiments were conducted over a period of about fifteen months with time out for summer vacation. During this period four dental examinations were made. Salivary analysis was done once every six weeks except during the summer. Wide variations were found in the calcium and phosphorus content of saliva of the same person at different times. No distinct difference in calcium and phosphorus range or average was found between the saliva of children free from caries and that of children having active caries. There was some evidence to indicate that caries-free persons secrete larger volumes of saliva than do those with active caries.

Supplementing the diet daily with 1 quart (946 cc.) of milk and 2 ounces (59 cc.) of tomato juice, with or without viosterol, tended to decrease slightly the incidence of dental caries. However, the improvement in the dental condition was not accompanied by any consistent change in the salivary calcium and phosphorus.

MUNNS, Winnetka, Ill.

ELKS CRIPPLED CHILDREN'S CLINIC. F. W. BUCKLEY, Nebraska M. J. **17**:289 (July) 1932.

The writer reports the work of the state Elks Association in sponsoring crippled children's clinics in Nebraska. The objectives are: (1) to provide an opportunity to all crippled children in Nebraska for a thorough orthopedic examination; (2) to assist in working out a plan for the treatment of those unable to bear their own expense, and (3) to aid in securing education and vocational training for handicapped children. They have divided the state into nineteen districts. A survey was made of the probable number of crippled children in the state. From an area containing approximately 40,000 people, and in which, from existing records, there were known to be thirty-seven crippled children, ninety cases were discovered. In other areas larger numbers of cripples than had been anticipated were similarly discovered. Based on such figures as are now available, it is estimated that there are three thousand crippled children in the state. At least 25 per cent of them need financial aid if treatment is to be undertaken. Congenital disability ranks first in number; poliomyelitis, second.

HAMILTON, Omaha.

BILATERAL PYOSALPINX FOLLOWING VULVOVAGINITIS IN A GIRL OF FIVE YEARS. DECHERF, Bull. Soc. d'obst. et de gynéc. **21**:198 (March) 1932.

A child had had leukorrhea for several months. For three weeks she vomited occasionally, and had frequent urgency and pain on urination. On palpation there was found a rather firm, somewhat tender mass below the umbilicus. The roentgenogram showed a dark shadow in this region. The temperature was 39 C. (102.2 F.). On exploratory laparotomy there was found a huge bilateral pyosalpinx filling the pelvis minor with numerous adhesions of the small intestine. The mass was incised and drained, and the child recovered. The vulvovaginitis, the nature of which was not stated, yielded to ordinary treatment.

GLASER, Rochester, N. Y.

EMPYEMA IN INFANCY. J. J. BINDSCHELDER and B. TASSOVATZ, Rev. franç. de pédiat. **8**:507, 1932.

Empyema is more likely to be encysted in infants than in adults. The diagnosis, therefore, depends on finding the localization. The general symptoms are pallor, anorexia and a continuation of fever following pneumonia. The final diagnosis is made by the roentgenogram. The treatment consists in evacuation by repeated punctures.

SANFORD, Chicago.

SURGICAL AND ORTHOPEDIC TREATMENT OF NERVOUS CONDITIONS OF SPASM IN THE LOWER EXTREMITY (STOFFEL'S OPERATION). PAUL DIETERICH, Rev. d'orthop. **19**:293 (July) 1932.

The numerous varieties of spasmodic conditions appear to offer clinical and experimental difficulties which are almost insurmountable. Many physicians and orthopedic specialists discourage active intervention. The prolonged use of plaster to combat the spasms is often poorly borne; the results of such treatment are mediocre, and recurrences are not overcome. Tenotomies, while freeing the spasm, leave a loose articulation and, in general, give poor results. Dieterich considers more active surgical intervention advisable and reviews the various operations on the nervous system. By the use of such surgical measures combined with orthopedic treatment, the prognosis in disease of the symptomatic-pachymeningitic motor system is rendered somewhat brighter.

CLARENCE A. RYAN, Vancouver, B.C.

OSTEOMYELITIS OF THE SPINOUS PROCESSES. F. LAGROT and L. COHEN SOLAL, Rev. d'orthop. **19**:311 (July) 1932.

Osteomyelitis of the spine most frequently affects the body of the vertebra. In this form the severity of the symptoms and the gravity of the prognosis are well

known. Invasion of the transverse or spinous processes is less frequent, and also less grave.

At the onset, there is intense pain due to the walled off abscess. Later, as the abscess extends in the fascial sheath, the pain becomes less. Eventually, the abscess comes to lie under the skin and, if not interfered with, breaks through. The result is a long-continued discharging sinus. However, if the abscess is opened thoroughly, the sequestrums removed and the abscess site packed with gauze, cure occurs within two or three weeks.

On examination, the spine is rigid, with a localized point of intense pain. At the end of a week, the pain more or less subsides, and the patient can lie on the bed. Spasm is lost, but localized pain persists, and the swelling is much larger, invading the opposite side, and it fluctuates. If intervention is not done, the skin becomes red and spontaneous rupture occurs, leaving a draining sinus persisting for months.

In differential diagnosis three conditions must be considered: (1) acute osteomyelitis of the body of the vertebra, (2) perinephritic abscess and (3) Pott's disease. In acute osteomyelitis of the vertebral body, the general health is markedly affected; a marked decline occurs, and there is little doubt of the diagnosis after the second or third day. In perinephritic abscess, the temperature is higher; the abscess lies in the vertebral gutter, and the area is slightly contracted at the onset. If puncture is done, a frank staphylococcus growth is found.

CLARENCE A. RYAN, Vancouver, B. C.

TREATMENT OF SCOLIOSIS BY A LATERAL PLASTER BED. JEAN HOCHE, Rev. d'orthop. **19**:331 (July) 1932.

Scoliosis is the most difficult of all the bony deformities to treat. Two factors are always at work: (1) atony of the structures and contractures of the muscles and (2) softening of the bony framework. These are accompanied by pallor, asthenia and anorexia. A vicious cycle is set up, contractures and rachitic deformities resulting. The abnormal pressure on the deformed side slows the rate of growth on that side, and the relaxed pressure on the opposite side stimulates an overgrowth. Therefore, the treatment must be directed against these two factors. This is best accomplished by gymnastics and orthopedic measures. Contraindications to gymnastics are persistent pain and rapid accentuation of the curve of deformity. A short rest period, however, usually suffices to overcome the pain, and it is seldom that mobility of the spine cannot be obtained by exercises.

Weight-bearing in a corrective corset does not give good results since such a corset tends to restrict the growth and to limit respiratory development. The author describes a plaster bed in which the patient is held on the healthy side in an overcorrected position during the night. This leaves the respiratory movement free and helps to build up the weakened side. During the day, a corset may be used after the deformity is somewhat corrected by the bed. Gymnastics are continued throughout the treatment.

RYAN, Vancouver, B.C.

PURULENT PLEURISY WITH PLEUROPULMONARY HERNIATION IN AN INFANT. GENEROSO A. SCHIAVONE, Arch. argent. de pediat. **3**:549 (Sept.) 1932.

This condition occurred in an infant aged 14 months, following an injury to the left anterior portion of the chest. A pleuropneumonia developed after the injury and in the course of a few weeks became purulent. A herniation about the size of an orange developed over the upper left anterior part of the chest at the end of the third month.

Three factors favored the development of the hernia, namely, the pleurisy with partial destruction of ribs due to a purulent pleurisy, the development of a pyopneumothorax and severe cough.

The cavity was evacuated successfully, but the case ended fatally.

SCHLUTZ, Chicago.

APPENDICITIS SIMULATED BY INTESTINAL PARASITES. C. INCLAN, Arch. de med. infant **1**:59 (Feb.) 1932.

In Cuba, intestinal parasites, such as Ascaris and Trichocephalus, are present in children much more frequently than is believed by many physicians, particularly in the rural areas. They produce a picture which simulates appendicitis and must always be ruled out before a diagnosis is made. The differential blood count is of considerable value.

SANFORD, Chicago.

OPERATION FOR UNDESCENDED TESTICLE (METHOD OF BEVAN). CARLOS URRUTIA, Rev. chilena de pediat. **3**:268 (July) 1932.

Operative procedure for undescended testicle should be undertaken before puberty. This will prevent degeneration and atrophy of the gland. The rapidity with which degeneration and atrophy take place depends on the degree of pressure. It is particularly liable to occur in inguinal ectopia of the testicle. If the undescended testicle is combined with inguinal hernia, an operative procedure to relieve both should by all means be undertaken. The operation advocated by Arthur Bevan is the operation of choice.

SCHLUTZ, Chicago.

REMOVAL OF ASPIRATED FOREIGN BODIES BY THORACOPNEUMOTOMY. REPORT OF FOUR CASES. A. FROMME, Beitr. z. klin. Chir. **153**:321, 1931.

In most cases the removal of aspirated foreign bodies can be done satisfactorily with bronchoscopy; yet the author concludes that thoracopneumotomy is indicated in individual cases, especially when a foreign body is found in small bronchi or bronchioles. The exact position of the body should be known; bodies of the metallic type are especially suitable.

The author removed three ordinary needles and one safety pin by the surgical procedure of Sauerbruch, which he describes. Two of the cases showed no complication. There were one with a mild and one with a severe pleural complication. All the patients recovered.

RUBIN, Boston.

A CASE OF EMPHYSEMA OF THE SKIN DUE TO OSTEOMYELITIS OF A RIB IN A YOUNG INFANT. OTTO ANDRESEN, Jahrb. f. Kinderh. **135**:335 (May) 1932.

Following an attack of nasopharyngitis, purulent osteomyelitis of the fifth left rib developed in a 7 week old infant. Empyema occurred, with infection of the lung, extensive subcutaneous emphysema and necrosis of the subcutaneous fat. In spite of furunculosis and pyuria, recovery followed resection of the rib.

CLAUSEN, Rochester, N. Y.

UROLOGY IN PEDIATRICS. W. BAUMANN, Monatschr. f. Kinderh. **54**:85, 1932.

This article, 100 pages in length and containing 47 diagrams and roentgenograms, is extensive enough to be a monograph. The writer argues that just as in "bronchitis" the microscope, the x-rays and instillations of iodine into the trachea are all used to rule out factors of tuberculosis or bronchiectasis, the diagnosis of pyuria is incomplete without the employment of additional diagnostic aids. He uses both the intravenous and the retrograde methods of pyelography, but his main thesis favors the latter technic. He shows many interesting roentgenograms and reports cases in which this method has aided in the outlining of normal kidneys and those involved by acute pyelitis. Pictures are shown of the kidneys in chronic pyelitis, hydronephrosis, infected hydronephrosis, pyonephrosis, renal abscess, renal tuberculosis, diseases and abnormalities of the ureters and diseases of the renal pelvis.

He devotes a few pages to functional tests of the kidneys and, owing to the time consumed in the tests, has discarded phenolsulphonphthalein, phlorhizin and diastase determinations. In his experience, the indigocarmine test has proved most

reliable. Within from six to ten minutes after the intramuscular injection of this dye, it should appear in the urine, and it reaches its maximum excretion in from ten to twenty minutes.

GERSTLEY, Chicago.

STUDY OF TREATMENT OF PLEURAL EMPYEMA IN CHILDREN WITH ETHYLHYDROCUPREINE. JAROSLAV PROCHAZKA, Časop. lék. česk. **69**:1633 (Nov. 28); 1673 (Dec. 5); 1709 (Dec. 12); 1755 (Dec. 19); 1790 (Dec. 26) 1930.

The author reviews the literature on the conservative and the surgical treatment of empyema. Treatment with ethylhydrocupreine has developed after its bactericidal action on pneumococci was discovered. The important factors are: puncture and lavage with ethylhydrocupreine; improvement due to antiseptic action or mechanical lavage, and effect of virulence on the course of the disease. Fifty-five patients ranging from 4 months to 9 years of age were studied; the results in five of them were not tabulated because the pus obtained was less than 100 cc. The treatment consisted of puncture, and when the pus was too thick thinning with 0.5 per cent solution of ethylhydrocupreine was used. Lavage with 0.5 per cent solution of this drug was carried on until the fluid was returned almost clear. In one case with 1,500 cc. of pus lavage was not attempted, because of possible toxicity from large quantities of the drug. After aspiration, a few cubic centimeters of 5 per cent solution of ethylhydrocupreine was instilled. Five patients required subsequent resection, and in two cases in which there was no response resection caused healing in fourteen and twenty-eight days, respectively. Sterilization of the discharge is questionable, as shown by subsequent puncture in some cases. The action of ethylhydrocupreine in vivo and in vitro is compared, and the significance of the acidity of the discharge was studied, as was also the effect of the virulence of pneumococci. This drug is of value in the treatment of empyema, although its value does not depend entirely on its bactericidal effect. Even when concentration is used which produces essentially 1:1,000 solution in the pleura (bactericidal in vitro), subsequent puncture reveals viable pneumococci. Continued use of ethylhydrocupreine does not lower the virulence of pneumococci, but in fact seems to increase their resistance. In no case was the acidity of the discharge sufficient to inhibit the growth of pneumococci. The effect of the treatment is the cleansing of the pleural cavity perhaps, as healing was obtained in two cases by lavage with distilled water.

The virulence of pneumococci judged experimentally is no criterion as to the progress of the empyema. Healing by lavage is possibly due to removal of the organisms and their toxic by-products. Each patient should be treated individually according to his condition and reaction. In children less than 2 to 3 years of age, the conservative puncture and lavage method is the treatment of choice. In older children (from 4 to 9 years), resection was indicated more often because the conservative method failed. Early aspiration is important in preventing debility of chronic absorption.

STULIK, Chicago.

OBSERVATIONS IN 634 CASES OF EMPYEMA AT ST. ANNE'S HOSPITAL. H. FRENKLOWA and N. A. MARGOLISWA, Pediat. polska **9**:381, 1932.

The 634 cases comprise 4 per cent of the general admittance to this hospital; 275 cases, or 43 per cent, occurred in children under 2 years of age. The mortality in this group is 71.3 per cent. Two methods of treatment were used: (1) the open method with rib resection and (2) the closed method, aspirators being used, with irrigation and suction. The prognosis in empyema depends on many factors. Most important is age; the older the child, the less the mortality. In treating these cases, Frenklowa and Margoliswa came to the conclusion that the conservative closed method should be used, because with the open method mortality was much greater.

KRUPINSKI, Chicago.

Miscellaneous

A Clinical Study of "Toledo's Strong Boy." W. E. McClure and B. Goldberg, J. Abnorm. & Social Psychol. **27**:159 (July) 1932.

The authors present the case of Clarence Kehr, a boy who, since the age of 4 years, has attracted nationwide attention because of precocious physical development and unusual physical strength. When he was first observed at the Juvenile Adjustment Agency, he was 5 years and 5 months of age. His general bodily structure was exceptionally large; he weighed 28 pounds (12,700 Gm.) more than the average boy of corresponding age and height. The sexual development was equivalent to that of a boy of about 14 years of age. Roentgenograms of the wrists and hands taken at the age of 5 years and 7 months revealed an anatomic growth equivalent to that of a boy 16 or 18 years of age. The dental development, interestingly, paralleled his chronologic age. Mentally, the boy showed an intelligence quotient of 92 at the age of 5 years and 5 months and one of 93 at the age of 6 years and 5 months on the Binet-Simon tests, rating thus below his chronologic age. He gave even poorer results on the Pintner-Patterson, Porteus maze and the Whipple-Healey tapping tests. The precocious physical development of the boy is thought to be due to a tumor of the pineal gland.

Abramson, New York.

Child Guidance Work in a Public Hospital. J. F. Williams, M. J. Australia **2**:294 (Sept. 3) 1932.

The author endeavors to show that the nervous and mental ailments of childhood are a part of the sphere of the general practitioner. Further training and interest in this work and cooperation with the psychologist and social worker are necessary to prevent loss of this important function to the medical profession.

Gonce, Madison, Wis.

Proceedings of the German Pediatric Society. Monatschr. f. Kinderh. **56**:1 (Jan.) 1933.

The forty-third session of the German Pediatric Society opened in Vienna, on Sept. 22, 1932, with Freund of Breslau presiding.

Noeggerath reviewed the subject of cystitis in infancy, reporting the interesting observation that changes in the mucosa of the bladder can be observed through the cystoscope when the buttocks of the infant are exposed to cold. He reported cases and entered into the discussion expressing the opinion that often cystitis is merely the result of chilling. He is skeptical of any treatment other than the administration of large quantities of water and the stimulation of the kidneys with potassium citrate. Lichtenberg gave a comprehensive review of the literature on the subject. It is questionable whether any urinary antiseptic is efficacious. Frick showed interesting roentgenograms of the kidneys, contrasting the pictures taken in the presence and in the absence of intestinal gas when the kidneys are outlined by intravenous medication. Pictures become strikingly clear if gas is removed from the intestine by the administration of 1 teaspoonful of animal charcoal in each of the two feedings preceding the test along with an enema consisting of 300 cc. of water and a teaspoonful of charcoal.

The second session was opened by Gottche. He reported an epidemic in which the rash and other symptoms were like measles, except that the onset was sudden, with a high fever lasting for seven days. At the end of the seventh day, a measles-like exanthem developed, which was lighter in color than that of typical measles. He classified the disease as "exanthema subitum," which was described by American writers in 1921. Teveli studied the conjunctival secretion bacteriologically in an epidemic of grip. Influenza bacilli were constantly found, even in the patients who showed a measles-like exanthem. Leitner reported favorably on the use of scarlet fever antitoxin as well as on the reliability of the Dick test. Bayer stated that he was disappointed in the use of vaccine for whooping cough. Wiskott dwelt on

the infrequency of pneumonia in early infancy, and he explained it as being due to the protective action of breast milk. Von Kiss reported the results of electrocardiographic studies of infantile grip. In the first stage there is extreme irritability of the whole conduction system, leading to tachycardia sometimes of a rate of 200 per minute. In this stage suprarenalin is absolutely contraindicated. In the second stage definite abnormalities develop as specific lesions occur in the heart. The electrocardiogram reflects these abnormalities. Fanconi reported a case of spontaneous galactosuria in a child with neurofibromatosis (von Recklinghausen). The child could tolerate all sugars except galactose.

The third session was opened by de Rudder, who reviewed the literature on the clinical effects of climate. He stated that one should not confuse seasonal variations with local disturbances. Moll continued the review, stating that climate affects not only mankind but animals and plants. He attempted to make an outline of the diseases to be treated by variations in altitude from sealevel to a level of 5,000 feet (1,524 meters), including the indications and contraindications. Koeppe showed that sunlight enhances iodine metabolism. Mommsen and Kielhorn studied pneumonias in reference to local atmospheric conditions. In Frankfurt, during the years 1929-1931, it seemed that pneumonia increased when the winds swung around to the north. The explanation is not so simple as it seems, for the increased morbidity always seemed to develop a day or two preceding this change. Jenny discussed diurnal variations in the frequency of birth, showing that the majority of children are born at night. Brock reported a series of measurements on the growth of children.

The fourth session was opened by Opitz, who agreed with the Americans who reported that blood transfusions are of value in certain chronic infections. For empyemas he gave blood intramuscularly; for long-standing bronchopneumonias he prefers the intravenous method. Favorable results are also reported in infectious diarrheas and in nutritional disturbance. Ullrich reported two interesting cases. Both children, following repeated infections of the upper respiratory tract, were brought to the hospital with a blood picture of agranulocytosis. Repeated transfusions of blood helped recovery. Eight weeks after their discharge, they returned again with mastoiditis. In spite of all treatment, the general condition became rapidly worse. One still showed agranulocytosis; the other, eosinophilia of 28 per cent, with extreme lymphocytosis. Both cases ended fatally. The writer expressed the belief that these cases are manifestations of abnormality of the reticulo-endothelial system, and he suggested that other diseases now classed as diseases of the blood may really be due to defects in that system. Freund showed mechanical devices to facilitate the making of roentgen examinations in small children. Weiss showed that the infant's body contains a brown as well as a white fat. The brown fat is the younger form.

Benjamin and Hinst reported a case of pyknolepsy in which the attacks occurred following any unpleasant experience, and they expressed the belief that the symptom is a defense mechanism. Lenart and von Lederer described the parathormone test for epilepsy. One unit per kilogram of body weight is given to a total of 10 for infants and 25 for older children. Eosinophil counts are made before the injection and five hours later, and the percentage of eosinophils in relation to the total leukocyte count is calculated. Normally, the parathormone causes a diminution of eosinophils. There is a definite difference in the varying percentages obtained in various diseases of the nervous system. A table shows that in true epilepsy there is a variation of under plus or minus 20 per cent, while in hysteria, variations of over plus or minus 30 per cent occur.

Nitschke, in experiments on rats, showed the importance of the thyroid gland in the metabolism of rickets. Vitamin D was ineffectual in thyroidectomized animals. Heymann showed that the absence of biliary secretion does not interfere with the efficacy of vitamin D. Gerstenberger reported cases of rickets associated with cirrhosis of the liver.

Catel, who has made experiments in vitro, claimed that ideas about the irritating properties of the lower volatile fatty acids on the intestinal musculature must be revised. Suranyi showed that in some cases of alimentary intoxication there was

an increased viscosity of the blood, while in another group there was not. Czapo divides acidosis into five groups: (1) ketogenic, (2) retention (from insufficient water or kidney insufficiency), (3) toxic (chemical or bacterial), (4) retention-toxic and (5) ketogenic-retention. Torok showed the importance of the liver in the metabolism of sodium chloride. He expressed the belief that the liver of the infant maintains a depot of sodium chloride which regulates the amount in the circulating blood. Kerpel-Fronius gave a warning against the danger of hypochloremia in cases of severe vomiting or diarrhea.

The German Association for Infant and Child Welfare met immediately following the German Pediatric Society. The program was devoted to tuberculosis. Hamburger discussed the influences of heredity, environment and natural immunity on the course of the disease. While he grants the great importance of hygiene and diet, he stated that one must not underestimate the importance of specific immunity, as the first infection is usually more serious than subsequent reinfections. Opitz reports the treatment of patients with open tuberculosis by ordinary welfare methods. He expressed the belief that much can be done for the children in these stations. Although the results obtained with pneumothorax were not brilliant, he believes they are somewhat better than those obtained by the more conservative methods.

Langer made a plea for more careful study and thorough treatment of tuberculosis of the bronchial glands. Duken made an effective plea for not squandering money in building great institutions for combating tuberculosis. He expressed the belief that better results can be obtained at much lower cost by sending children to inexpensive camps fitted up especially for them in regions offering favorable climatic conditions.

GERSTLEY, Chicago.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

HUGH MCCULLOCH, M.D., *Secretary*

Forty-Fifth Annual Meeting, May 8-10, 1933, Washington, D. C.

OSCAR M. SCHLOSS, M.D., *President*

(Concluded from page 461)

RÔLE OF ACIDOSIS AND ALKALOSIS IN THE ETIOLOGY OF RICKETS. DR. BENGT HAMILTON and DR. CHARLES SCHWARTZ (by invitation), Chicago.

Rickets was completely prevented in animals on a rickets-producing diet by the addition of acid sodium tartrate to the diet, thus causing intestinal acidity and metabolic alkalinity. Rickets was produced on a nonrickets-producing diet by the addition of a mixture of ammonium chloride and ammonium carbonate, thus causing intestinal alkalinity and metabolic acidity.

DISCUSSION

DR. DANIEL C. DARROW, New Haven, Conn.: I should like to ask Dr. Hamilton whether he has determined the intestinal p_H.

DR. ALFRED T. SHOHL, Cleveland: I think that Dr. Hamilton's presentation is very interesting, in that for the first time he has been able to separate the total acid phase of the diet into two component parts: absorption and acid-base economy. I think that he has shed a great deal of light on this problem.

As Dr. Hamilton said, we have been able to show only that the results were to a certain extent conflicting. When the diet was too acid, bad results were obtained; as the neutral zone was approached, the absorption and degree of precipitation became better, and as the more alkaline zones were reached, the absorption became worse, so that the total effect was worse. We were able to show the acid-base effect only by so carefully regulating the diet that it was just borderline; Dr. Hamilton has been able to show these effects with gross differences.

There are several questions of a quantitative nature which I should like to ask Dr. Hamilton. How did he alter the calcium and phosphorus ratios and still obtain these results? Does he have quantitative data on the acid-base nature of the diets?

It is true that Zucker improved a rachitogenic diet by adding acid to it, but he told me at the time that if the amount of acid that is added to the diet is increased, the same cycle that I have described occurs. The additional amounts of acid render it less rickets-producing, and the addition of greater amounts causes rickets. I should like to ask how acid and alkaline the diets were in terms of excess equivalents of acid base.

DR. BENJAMIN KRAMER, Brooklyn: What was the calcium concentration of the serum?

DR. JULIUS H. HESS, Chicago: I wish to call attention to the difference in pathogenesis between rickets in infants and rickets in rats. If we are to apply this diet to infantile rickets, we have to think of the lack of absorption of phosphorus in infants.

Every rachitic diet is based on the fact that it has either an absolute or a relative lack of phosphorus, so that the rats do not receive this substance. With this method no infant ever has rickets. All infants in whom rickets develop have enough phosphorus in the diet. All infants are fed milk, which contains enough phosphorus, so that we have to be careful. As I said, Dr. Hamilton knows this as well as I do.

As to the difference in the pathogenesis, there is no lack in the supply of phosphorus in any infant, including those in whom rickets develops.

DR. A. A. WEECH, New York: When observations of this kind are described, the mind of the clinician always turns to the possibility of clinical application. It seems that this method of mixing salts so as to obtain one reaction in the intestine and another in the body fluid might be applied to the treatment of renal rickets or of endogenous rickets. Have such applications been attempted as yet?

DR. BENGT HAMILTON, Chicago: As to the first question, the p_H in the intestinal tract has not yet been determined. It is reasonable to assume, however, that the addition of acid or alkali to the diet will change the intestinal reaction in the direction of acidity or alkalinity. Dr. Darrow is right, however; it should be checked because the change in the reaction might not be as much as one would suppose; the buffer value of the milk and the change in the secretion of intestinal juices may counteract the effect. This is one thing that we have on our program.

The quantitative acid-base relationships of these diets are the same as those of the Steenbock rickets-producing diet and the Steenbock stock diet plus the added salts. They can easily be approximately calculated.

We have not yet determined the calcium in the serum. I agree with Dr. Hess that we should not apply these results directly to the diseases of infants. I have not attempted to do so, and I have been talking only about the effect of cod liver oil on rats. I think, however, that when we have collected enough data on animals, we can, with the greatest caution, begin to apply them to a human disease.

As to renal rickets, the suggestion is extremely interesting. I had not thought of it. One has to remember, of course, that tartrate is a salt with which one has to proceed carefully.

The changes in the internal reactions were as shown on the charts. There were no changes in the p_H but alkalosis and acidosis were present only as evidenced by changes in the bicarbonate content.

RENAL RICKETS WITH GENERALIZED CALCINOSIS AND PARATHYROID DYSFUNCTION. DR. FRANCIS SCOTT SMYTH and DR. LEON GOLDMAN (by invitation), San Francisco.

A 14 year old boy had been under medical supervision for two years following acute hemorrhagic nephritis. Our attention was called to his condition when marked weakness of the muscles of the legs and the pelvic girdle suggested progressive muscular dystrophy. Examination, however, showed a definite dwarfed stature, a subicteric tint to the skin, scanty hair, brittle, ridged nails and general hypotonia of the musculature. Laboratory data revealed an extreme loss of renal function (preuremic) and a remarkably elevated calcium and phosphorus content of the blood. Roentgenograms showed generalized demineralization. Studies of the excretion of calcium and phosphorus were made with the patient on an analyzed diet.

Continued observations over a period of six months showed progressive calcification of the arteries and falx and cystic masses at the chondral junctures, in addition to the demineralization of the normal skeleton. A diet consisting of alkaline ash with calcium gluconate was given without any apparent effect. Vitamin D was strictly avoided. The patient died. A complete postmortem examination revealed generalized calcinosis in the arteries, kidneys, fundus of the stomach, lungs, dura mater and other organs. The kidneys showed hydronephrosis with interstitial nephritis. The bones showed irregular trabeculation and were so soft that decalcification was unnecessary for preparation for microscopy. Five remarkably enlarged parathyroid glands were removed, which on section showed hyperplasia without adenomatosis.

(Slides were presented showing both the clinical course and the postmortem observations. The theoretical problems which the case illustrates were briefly discussed.)

Somewhat similar cases reported by Reginald Lightwood of London and Thomas B. Cooley of Detroit were compared with the case; these authors sent microscopic slides for that purpose.

DISCUSSION

DR. CHARLES ANDERSON ALDRICH, Winnetka, Ill.: I was much interested in Dr. Smyth's paper. About ten or twelve years ago we had a patient with renal infantilism at the Children's Hospital who had a similar swelling in one metatarsal joint. We performed an autopsy and found caseous material which we could not explain at the time. I have no doubt that it was the lesion Dr. Smyth demonstrated. This child had been ill for six years.

I should like to ask whether or not there was dwarfism before the apparent onset of the hemorrhagic nephritis.

DR. JULIUS H. HESS, Chicago: There is a paradoxical phenomenon to which I wish to call attention: the decalcification of the bone with the hypercalcification of the organs, in this case, in the kidneys, the lungs and the blood vessels. I believe that the hypercalcification is caused when the calcium and phosphorus are taken away from the bone. A case which I saw several years ago impressed me with this fact. It was a case of a little different nature, but there was decalcification of the legs and of the vessels of the lower extremities, but none of the upper extremities. I think that we felt that it was caused by a local transfer from the bone into the blood vessels.

DR. FRANCIS SCOTT SMYTH, San Francisco: I think that in our case there unquestionably was some dwarfing prior to our observation. We saw the patient for eight months, at the start of which he, at 14 years, had the stature of an 8 year old boy. There were also cystic masses on his fingers. I have a great many more slides but time does not permit presenting them. We also made studies of the magnesium phosphate and have a great many more bits of interesting information.

PHYSIOLOGIC DISTURBANCES IN DIPHTHERITIC INTOXICATION, WITH A NOTE ON THERAPY. DR. DANIEL C. DARROW and DR. HERMAN YANNET (by invitation), New Haven, Conn.

A study of the concentration of certain constituents of the blood and tissues of rabbits given injections of diphtheritic toxin revealed certain facts which aid in the interpretation and treatment of malignant diphtheria. A dose of toxin that kills rabbits in from two to four days produces renal lesions accompanied by azotemia, and hepatic necrosis accompanied by an increase in amino-acid nitrogen and low blood sugar. A dose that kills in from four to eight days produces less marked lesions of the kidneys, but the longer period of survival leads to a higher concentration of nonprotein nitrogen in the blood. In these rabbits the lesions of the liver are less extensive and are accompanied by hyperglycemia and little or no increase in amino-acid nitrogen. The glycogen of the liver is lower in diphtheritic rabbits than in controls, but no difference was demonstrated in the glycogen of the heart or muscles. A definite defect in the ability of the livers of diphtheritic animals to store glycogen was demonstrated. Diphtheritic rabbits show hemoconcentration accompanied by diminished electrolyte concentration and increased inorganic phosphate. This picture was thought to be analogous to shock.

Malignant diphtheria presents evidence of changes similar to those described. Early in the disease there is a generalized injury of the tissues, particularly of the liver, kidneys and vascular system. Later, cardiac symptoms dominate the picture, though hepatic insufficiency still plays a rôle. Late in the course, the chief symptoms are due to paralyses, though the cardiac disease may still be manifest.

Our work calls particular attention to shock, nephritis and hepatic insufficiency. In these conditions, parenteral injections of saline and dextrose and transfusions of blood are indicated. Attention is called to the fact that this treatment can be applied successfully for diphtheria. The handling of the persistent vomiting of malignant diphtheria apparently requires the withholding of all fluids by mouth and the administration of sufficient saline and dextrose by proctoclysis, hypodermoclysis and intravenous infusion to maintain diuresis. It is pointed out that in one patient such a regimen without the giving of fluid by mouth for eleven days was followed by recovery. Large amounts of dextrose solution may be slowly injected intravenously into a patient with marked cardiac decompensation.

Digitalis has been used without untoward results in our last three cases of diphtheritic myocarditis, apparently with a life-saving result in one of the patients. We believe that a small dose of digitalis (from 15 to 25 mg. per kilogram of body weight) should be given if marked congestive heart failure occurs. Digitalis, however, should be given when congestive heart failure develops and not in anticipation of cardiac failure.

FURTHER STUDIES ON THE USE OF THE KETOGENIC DIET IN THE TREATMENT OF URINARY INFECTIONS. DR. HENRY F. HELMHOLZ, Rochester, Minn.

The use of the ketogenic diet in urinary infections was approached from two standpoints at about the same time: (1) as a means of rendering the urine acid and (2) as a means of bringing into play something in the ketonic urine other than its acidity which rendered the urine bactericidal.

It has been shown in the study of several cases of infection of the urinary tract that by acidification of the urine with ammonium chloride the urine can be freed of pus and the patients relieved of their symptoms of frequency and urgency. It has been further demonstrated, however, that by the administration of ammonium chloride, the p_H of the urine can be maintained for days between 4.9 and 5.1 without any apparent reduction in the number of viable colon bacilli in the infected urine, but by the administration of a small amount of methenamine, the acidity of the urine remaining between 4.9 and 5.1, the urine can be sterilized. These therapeutic experiments are significant, for Niellson maintained that even if ketonic urine of low acidity did not kill bacteria in the test tube, the bactericidal effect was sufficient to clear up the urinary infection in vivo. He did not realize at that time that the bactericidal effect of ketonic urine depended on something other than its acidity.

The clinical results continued to be satisfactory. It has been possible to clear up all subacute and chronic infections for which the diet has been used, with the exception of cases in which nephrolithiasis has been present. In a recent case, after the urine had remained sterile for four days, severe sore throat and cervical adenitis developed, and on the following day there was a relapse, with the appearance of colon bacilli in the urine. Administration of the diet was discontinued temporarily, and on its resumption the infection cleared up without difficulty.

The boiling of bactericidal ketonic urine usually does not destroy its power to kill organisms. This proves in another way the experiments in which diacetic acid and sodium diacetone were added to urine of low p_H and were found to be without any bactericidal power. A 4+ test for diacetic acid was rendered negative by five minutes of boiling. Nevertheless, in sixteen of twenty-one experiments the boiled urine had the same bactericidal power as the unboiled specimens.

Dilution of ketonic urine renders it inert. The specimen with the highest bactericidal power was rendered inactive after a dilution of 1 to 4. Urine of weaker bactericidal power did not inhibit growth in a dilution of even 1 to 2.

Alkalinization of the urine to above p_H 5.6 in most cases caused the bactericidal power to disappear, although in one specimen it was possible still to show definite inhibiting power at a p_H of 6.4. When specimens are allowed to stand in the ice chest a gradual increase in the p_H is noted, and at a p_H of 5.8 the bactericidal power is usually gone. If the original p_H is then again established, the bactericidal power returns. Even so, there are ketonic urines of the same low p_H which have no bactericidal power.

In order to determine the length of time the ketogenic diet keeps the urine bactericidal, the bactericidal power of the urine was tested daily. After ten days, in spite of a p_H of 5.3 and a 4+ diacetic acid test, the bactericidal power had disappeared. Epileptic children who had been on a ketogenic diet for some weeks did not have urines with bactericidal power.

DISCUSSION

DR. ALFRED T. SHOHL, Cleveland: About twelve years ago we made studies on the effect of the acidity and alkalinity of the urine on the killing of Bacillus

coli and their antiseptic powers. We early convinced ourselves that the urine could be rendered acid enough or alkaline enough outside the body to prevent growth or to kill organisms when inoculated into the urine. The only difficulty was that we could not maintain the acidity in children or even in adults because the reaction of the urine was never low enough to come within the killing range.

It then occurred to us that we might perhaps get the organisms used to a medium close to the death point, shift to an alkaline medium and then perhaps, by the rapid change kill the organisms. But the organisms were too quick for us, and we never accomplished our aim. Therefore, we abandoned that principle of treatment except in conjunction with methenamine.

It is interesting to see that with this type of diet the acid-base effect is so important, and that the mechanism works, even by an as yet unexplained means.

DR. HAROLD L. HIGGINS, Boston: I should like to ask Dr. Helmholz whether he has done any work on the acidosis of starvation in overcoming urinary infections. In our cases in which the ketogenic diet was used we found that the p_H of the urine was higher at the beginning than later. Perhaps that fact parallels Dr. Helmholz' observations on the tonicity of the urine.

DR. HENRY F. HELMHOLZ, Rochester, Minn.: I have always been interested in Dr. Shohl's work on the effect of acid and alkaline reactions on bacteria in the urine. We performed similar experiments. Only occasionally did we find organisms that could be grown at a p_H of 8.4. We introduced them into an acid medium of p_H 5.3 or 5.4, and in no case did we obtain a lag for a period of more than from four to six hours. In no sense did we get anything that seemed worth while trying in treatment.

I wish to emphasize that apparently a low p_H of 5.1 or even 4.9, obtained by the administration of ammonium chloride, rendered the organisms more susceptible to the formaldehyde in methenamine.

I have reversed my opinion of methenamine once or twice, and it looks as though I have been going around in a circle, advising doses of from 50 to 90 grains (3.25 to 5.95 Gm.) in the treatment of urinary infections. Recently with a very acid urine I found that the administration of 1 or 2 grains (0.065 or 0.13 Gm.) of methenamine is sufficient to sterilize the urine. I have not been able to obtain this effect with urine at a p_H of from 5.1 to 5.

I believe, as Dr. Shohl does, that we are able to influence the ease with which we can kill bacteria, not by a change, but by keeping them at a low p_H.

With regard to Dr. Higgins' question, we have tried starvation in a number of instances. We have not felt that we could starve patients except as we had such patients available. As yet we have found no bactericidal power in the urine. Perhaps the p_H has not been low enough. We have found that there is an initial drop in the p_H in the first three or four days; this continues for the next three or four days, and then there is an increase.

In the particular chart I showed, the urine remained at a p_H of from 5.3 to 5.4, in which range there is usually definite bactericidal power. But in spite of that bacteria grew in the urine. We are trying to determine the bactericidal substance. It has been strange that we have tested a number of specimens of urine that did not show any bactericidal power. I believe that some of our difficulties are caused by the fact that the bactericidal power tends to disappear after from ten days to two weeks.

ETIOLOGY OF THE COMMON COLD. DR. A. R. DOCHEZ (by invitation), New York.

Studies of the etiology of the common cold have brought evidence indicating causative activity on the part of a variety of micro-organisms. These organisms include the ordinary bacteria of the upper respiratory tract, certain gram-negative anaerobic bacteria and the filtrable viruses.

The studies reported have indicated that visible bacteria of the respiratory tract are not the most important etiologic agents in the common cold. Studies of experimental transmission of this disease to apes and to human beings have brought proof of the existence of a filtrable virus capable, in the absence of all other bacteria, of producing typical experimental attacks of the common cold. A number of tissue

cultures of this virus have been made. These cultures have continued to produce typical examples of the common cold in human volunteers over a period of three years. The duration of immunity to the virus of the common cold is very short.

THE CARRIER RATE OF PATHOGENIC BACTERIA IN RELATION TO EPIDEMIC DISEASES OF THE UPPER RESPIRATORY TRACT IN INFANTS. DR. YALE KNEELAND, JR. (by invitation), New York.

For the past four years we have been studying the flora of the upper respiratory tract in infants at The Home for Hebrew Infants in New York City. This institution harbors a population of approximately 300 infants, ranging in age from 3 months to 3 years. The infants constitute a population semi-isolated from the outside world, but in close contact with one another; in each age group the opportunity for communication of pathogenic agents is good. There exists, as a result, a high incidence of diseases of the upper respiratory tract of all types throughout the year.

It has been observed that infants between the age of 8 and 14 months are most susceptible to the more serious forms of diseases of the upper respiratory tract, i. e., febrile disturbances associated with acute pharyngitis or tonsillitis, often with otitis media and cervical adenitis and not infrequently with pneumonia. We have followed the respiratory flora of this group, correlated with the clinical behavior, and have contrasted them with the flora of the older children (who appear to have a greater immunity to the complications of infection of the upper respiratory tract). The various diseases were divided into two rough groups, afebrile and febrile, that is, the common cold and the more serious diseases of the upper respiratory tract.

The first autumn wave of infection was chiefly of the type of the common cold, and was not found to be associated with any alteration in the bacterial flora; the carrier rate for pathogenic organisms was very low. As the season progressed, the carrier rate rose, and more febrile disturbances appeared. In two consecutive years a very high peak in the carrier rate for a single pathogenic organism was noted in the month of March, and this coincided with an explosive outbreak of disease of the upper respiratory tract. In the group of older children the outbreak consisted of approximately equal numbers of febrile and afebrile disturbances, but in the group of highly susceptible children, the expected increase in colds did not occur; in fact, only 1 child in this group had a cold, but more than half of them suffered from a more serious infection associated with fever. (The carrier rate for pneumococcus in this group was 95 per cent.) The inference was drawn that serious epidemics of disease of the upper respiratory tract may be caused by the agent of the common cold acting in conjunction with a widespread carrier state of a pathogenic bacterium.

Additional evidence for this hypothesis is afforded by an experiment performed this winter, wherein 20 members of the most highly susceptible group were given a long-continued course of injections of vaccines composed of Pneumococcus, Haemophilus influenzae and Streptococcus haemolyticus, 20 alternate infants being used as controls. A significant diminution in the number and severity of febrile infections was noted in the vaccinated group. The incidence of the common cold was not affected.

DISCUSSION ON PAPERS BY DOCHEZ AND KNEELAND

DR. JAMES DOWLING TRASK, New Haven, Conn.: Did Dr. Kneeland attempt to use what is considered as the highly parasitic form of bacteria in the vaccine? In other words, what kind of pneumococcus did he use? Did he attempt to include a smooth influenza bacillus or a mat hemolytic streptococcus?

DR. HENRY F. HELMHOLZ, Rochester, Minn.: The topic that has been brought up by Dr. Dochez and Dr. Kneeland is one of the most important that has been presented before this society in many years. Since through the efforts of preventive pediatrics we have practically wiped out the mortality from diarrheal disease, it seems to me that the great problem before us is this problem of the

common cold. It must be admitted that in the last fifteen years we have made practically no progress in controlling deaths from this disease.

I have had the pleasure of following Dr. Dochez' work since I was chairman of the committee of the Society for the Study and Prevention of Infant Mortality.

It has been interesting to see how the pendulum has swung from the virus to the bacteria, and I think that it is now permanently on the side of the virus, owing to the work Dr. Dochez has been doing during the past year.

For two years we have studied a series of children particularly as regards the incidence of hemolytic streptococci. If we had used merely the experience of our first year, we should have thought, too, that there was an increased incidence of the organisms in the nasal pharynx during the winter months; however, the following year there was a marked incidence of organisms, as I recall it 80 per cent, during August.

It seems that this work should stimulate further investigation along this line, and that this field in preventive pediatrics deserves our best efforts.

I wish to thank Dr. Dochez, in particular, for presenting this interesting subject.

Dr. A. R. Dochez, New York: There are, of course, fluctuations in the distribution of pathogenic organisms of the upper respiratory tract. An increased incidence of organisms is not always associated with an increase in disease of the respiratory tract. The epidemiologic significance of this fact is not understood at present. Dr. Coburn has observed examples of increased distribution of hemolytic streptococci which have not been associated with evidence of an increased amount of streptococcic infection. Whether or not the organisms in these examples were of low virulence one cannot say. When we have perceived definite examples of increased pathogenic activity on the part of the organisms, it has usually been in association with an outbreak of common cold or other infection of the upper respiratory tract. A recent study of readmissions to the Presbyterian Hospital for decompensation in rheumatic heart disease showed that 50 per cent of the breaks followed an attack of infection of the upper respiratory tract. It is a matter of experience that the common cold or influenza may provoke exacerbation of a pathologic process in the organs remote from the respiratory tract. It seems that the virus of the upper respiratory tract opens the door to bacterial infection. This bacterial infection may express itself predominantly in the respiratory tract itself, or in some instances the effect may be most manifest in distant organs, such as the heart and kidneys.

Dr. Yale Kneeland, Jr., New York: In reply to Dr. Trask, the vaccine which I employed was the pneumococcus type I, S. I used that vaccine because there was wide heterogenicity in the types isolated, and from experimental work on animals I felt that a single type would give rise to a fairly solid active immunity against the other types. Pfeiffer's bacillus vaccine consisted of equal portions of Pitman's A and B smooth strains. The streptococcus was the N. Y. 5 strain; two strains were obtained from Dr. Coburn, and one strain was that which Dr. Dawson uses for his agglutination tests in rheumatoid arthritis.

In connection with the fact that we used the N. Y. 5 strain in the vaccine, it is interesting to note that during the course of what was apparently an epidemic of typical scarlet fever, scarlet fever developed in two of the infants vaccinated with the N. Y. 5 strain, as well as in two or three of the children in the control group.

Pelvirectal Achalasia (Hirschsprung's Disease): Temporary Medical Management by Rectal Administration of Magnesium Sulphate. Dr. Barnet E. Bonar, Salt Lake City.

This article will be published in full in a later issue of the American Journal of Diseases of Children.

The Motion of Growth: XVI. Clinical Aspects of Growth and Metabolism. Dr. Norman C. Wetzel (by invitation), Cleveland.

From the clinical side, attention is focused on three principal phases of growth: (1) the event of growth itself, (2) the supply of nutriment and (3) the processes

of energy consumption. A dynamic relationship between the events of growth and metabolism has recently been described on which the present clinical interpretations are made to rest. Subject to these constraints, growth is regarded as a mode of motion, the essence of which is change in size per unit size.

Energy for growth is distributed and utilized in five different ways: (1) new cells, (2) storage, (3) momentum, (4) dissipation and (5) for cellular proliferation. It is evident that growth is insufficiently described by merely detailing successive changes in size. One needs, in addition, to learn that some substance, x, promotes growth, and also to find out how this substance affects each of the foregoing five properties of growth.

Energy for maintenance refers only to tissue physiologically at rest, that is, to tissue in a state of pure and simple existence. The production of basal heat in growing subjects must always exceed that in subjects in whom growth has ceased; the higher metabolism of infants is caused, therefore, by the fact that they are immersed in the flux of growth.

The dynamic overload of growth in premature infants under conditions of extrauterine life is a major factor in the difficulty of raising such infants.

The physiologic loss of weight at birth is an accidental and not a fundamental event in the career of all new-born infants.

Excessive rates of gain in infancy are followed by corresponding delays in growth; they tend, in addition, to increase energy loss and waste.

Growth and metabolism are at low tide during the preschool phase of life. I am inclined to infer that the physiologic basis of anorexia is to be found in the relatively low demand for energy on the part of a healthy organism during the very years in which there is comparative rest in the motion of growth.

DISCUSSION

DR. FRITZ B. TALBOT, Boston: In connection with this work we should remember Dr. Wetzel's distinction between growth and motion of growth. His conception is quite different from ours as pediatricians.

I see in his chart that the motion of growth continues until at least 32 years of age, whereas my conception as a pediatrician of gain in weight and height is that it finishes somewhere between 16 and 18 years in girls, and a bit later in boys.

I became interested in the question of growth in relation to basal metabolism this spring. I am making a study of our original data and new data which have not yet been published, with the hope that the element of growth, whatever way one may care to look at it, may play some part in explaining the rise in metabolism which is usually found during puberty.

DR. HAROLD C. STUART, Boston: I should like to add one suggestion along the line of Dr. Talbot's discussion; possibly the difference between the age curves for metabolism and growth can be explained on the basis of individual variations. We know that there are such variations at all ages but that they are particularly marked at the time of puberty and during the adolescent period. There are some children who apparently attain their adolescent growth in a year or six months, whereas in some the process is spread over a period of three or four years.

It seems obvious that if this spurt of growth is completed within six months or a year, the metabolic rate may be altered temporarily, whereas if it is spread over a period of years at a slower rate of gain, there would be no noticeable change in the metabolic rate. A curve of average rates per year of age would mask these relationships.

DR. SAMUEL W. CLAUSEN, Rochester, N. Y.: I understand that the differential equations that have been shown describe the motion of growth on the average, and that these equations contain certain constants which perhaps characterize the average person.

I wonder whether it is possible, by plotting the curves of a person, to ascertain the values of the constants and therefore to obtain certain constants which are

characteristic of that person's constitution. In that way one could obtain data which might be of use in the prediction of the clinical condition of that person in the future.

DR. NORMAN C. WETZEL, Cleveland: I should like to say first that those of us who are interested in the mathematical side of the problem have a certain feeling of confidence when we deal with and turn to data such as those of Dr. Talbot and his associates. We feel that we are standing on extremely firm ground.

It is true, as Dr. Talbot pointed out, that height and weight do not show up simultaneously; there is, as a matter of fact, not much increase in height after from 16 to 18 years of age, although weight continues quite definitely to increase for a number of years afterward.

The reason for using mass rather than length, or some function of length, is chiefly because the physicists assured me that mass is much more easily, more correctly and more reliably measured than height. Both of these indexes of size, however, are connected with the property of density, and from the theoretical standpoint it really makes no difference in the last analysis whether one determines size as a function of mass or as a function of surface, or even of length, so long as the density remains the same.

Dr. Clausen raised a particularly interesting question. We have had the opportunity to study individual growth curves, so to speak, but the unfortunate part of some of this work is that in order to make any analysis worth while it is necessary to have data that are especially reliable. It so happens that data on individual subjects vary so widely that one is not able to place nearly so much confidence in them as one can do with the data Dr. Talbot collected.

Another difficulty also arises. The calculation of the fundamental quantities in the differential equations requires about six weeks' labor, so that at the present stage of the work we have not felt that the results would be justified. We are dealing with a child whom we pediatricians loosely call normal, although we understand fairly well what is meant by that term. Once the constants for the normal child have been properly obtained, it will be possible, if we are able to collect suitable data, to compute the constants of children who deviate from the normal as regards oversize or undersize, on the one hand, and excessive and unsatisfactory rates of gain, on the other.

GUANIDINE AS A COMPLICATING FACTOR IN CERTAIN CONDITIONS IN CHILDREN. DR. HORTON R. CASPARIS and DR. ANN MINOT (by invitation) Nashville, Tenn.

Our interest in guanidine as a probable complicating factor in certain children was first aroused about three years ago on the observation of the symptom complex presented by dogs poisoned with guanidine. Minot had found high guanidine levels in the serum of dogs whose livers had been acutely and extensively damaged by carbon tetrachloride. These animals became restless and vomited brown material; diarrhea developed, and then twitching of the muscles, followed by what appeared to be typical tetany with convulsions. In the more severe cases coma and death resulted.

During the hyperexcitability, the typical electric reactions of tetany were obtained in the presence of normal serum calcium and mild to moderately severe acidosis. The same high guanidine levels and the same symptom complex and blood findings could be produced by subcutaneous injections of sufficient amounts of guanidine into normal dogs.

On noting the similarity of this train of symptoms to that seen in some of our severely sick infants, we suspected that guanidine might be a complicating factor in their conditions. After making hundreds of determinations of guanidine during the past three years in infants and children with a variety of disease conditions, we are convinced that one will find high guanidine levels in the serum of all infants who have been rapidly and extensively dehydrated. Increased amounts have been found in some patients with severe and extensive secondary pneumonia and also in children who have been burned extensively. The normal guanidine content of

the blood varies from 0.3 to 0.4 mg. per hundred cubic centimeters of serum. Symptoms which we attribute to guanidine poisoning appear as the guanidine level in the blood passes beyond 0.6 or 0.7 mg. per hundred cubic centimeters of serum.

The symptoms associated with guanidine poisoning produced experimentally are referable mainly to the gastro-intestinal tract and to the central nervous system.

Postmortem examinations of these animals reveal hyperemia of the gastro-intestinal tract with small bleeding points. The central nervous system and other organs, including the kidneys, are congested, and often there are varying degrees of extravasation of blood. We have seen these changes at autopsy in infants who during life had high guanidine levels in the blood.

The question then arises as to what guanidine is and what its source is. Guanidine is a nitrogenous base with the formula $NH:C(NH_2)_2$. This group occurs in creatine (methyl-guanidine acetic acid) and in amino-acid arginine (lamino-5-guanidine valerianic acid), but more than that we do not know. We suspect that the source of guanidine is in the breakdown of tissue, as it occurs in high levels in the blood following severe burns, acute extensive injury of the liver and extensive tissue necrosis, experimentally produced, and in connection with acute and extensive shifts of fluids from the tissues into the blood stream. Thus it is seen that its occurrence above normal levels or in toxic amounts in the blood stream is secondary to some primary cause.

It is well known from the work of Staub and others that the action of guanidine and calcium is antagonistic. Further evidence that we are dealing with guanidine or a guanidine-like substance is offered by the fact that when an excess of calcium is maintained in experimental animals and in children, the symptoms and findings which we have attributed to guanidine poisoning can be prevented or relieved.

Again, the occurrence of guanidine in increased amounts in the blood is secondary to some primary cause. The smaller increases can be handled adequately by the organism, especially if the previous mineral metabolism has been good, but when large amounts of guanidine occur in the blood we believe that the toxic action must be combated with excess calcium in order to get the best results from the other necessary measures that are commonly employed in treating such patients. In fact, we believe that in some instances the toxic effects of guanidine are sufficient to explain some of our failures to get results in spite of the fact that all well recognized means of treatment have been employed.

VEGETABLE FEEDING IN THE YOUNG INFANT: INFLUENCE ON GASTRO-INTESTINAL MOTILITY AND MINERAL RETENTION. DR. FREDERIC W. SCHLUTZ, DR. MINERVA MORSE (by invitation), and MISS HELEN OLDHAN (by invitation), Chicago.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

TUMORS OF THE BRAIN IN CHILDREN. DR. HARVEY CUSHING (by invitation), Boston.

Dr. Cushing spoke briefly on tumors of the brain in children. He emphasized the comparative frequency of midline cerebellar tumors which in the past few years pediatricians have come to recognize. He spoke of the fact that many patients with such tumors are highly favorable risks for surgical intervention, as the tumors represent a benign type of glioma. He also mentioned other types of tumor of the brain encountered in childhood.

THE COMPOSITION OF PRIVATE PEDIATRIC PRACTICE: INCLUDING A METHOD FOR KEEPING ADEQUATE CLINICAL RECORDS. DR. CHARLES ANDERSON ALDRICH, Winnetka, Ill.

This article will be published in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

FACTORS AFFECTING THE UTILIZATION OF CARBOHYDRATE WITH PARTICULAR REFERENCE TO RECURRENT VOMITING. DR. J. A. JOHNSTON (by invitation), Detroit.

Following an isolated observation that the respiratory quotient failed to show any appreciable rise after the intravenous injection of dextrose into a patient who was just recovering from a severe attack of vomiting, various studies were carried out over a period of five years to evaluate critically the factors affecting the oxidation of carbohydrate.

It was shown that not only does a complete fast obliterate oxidation and increase storage, but oxidation can be quantitatively related to any level of glycogen if it is granted that the basal metabolic mixture reflects the level of available glycogen. There is an absolute correlation between the amount of dextrose available from the protein fat and carbohydrate of the basal metabolic mixture and the amount of intravenously injected dextrose oxidized over a given period.

Changes in the reaction of the blood affect oxidation in the following manner: Moderate acidosis increases and moderate alkalosis diminishes oxidation. When the administration of alkali is pushed to the point of diuresis, however, oxidation is again increased. The effect of the acidosis is probably the result of an increase in glycogenolysis, and the effect of alkali is the converse of this, glycogenolysis being optimum slightly to the acid side of neutrality.

Infection		20
Tonsil	10	
Sinus	2	
Teeth	1	
Liver and gallbladder	5	
Appendix	2	
Malnutrition		11
Emotion		10
Fatigue		3
Postural defect		2

Evaluation of the thyroid effect suggests confirmation of the current idea that hyperactivity of the gland results in increased glycogenolysis, while the suppression of function is accompanied by a delay in glycogenesis, but that there is no direct antagonistic relation between the thyroid and insulin. The ultimate effect, however, differs from the immediate effect as it does with acidosis in that a prolonged hyperactivity completely depletes the glycogen reserve and obliterates oxidation of the administered dextrose.

Studies on a group of children subject to recurrent attacks of vomiting brought out the fact that in this series there was no single metabolic disorder characteristic of the entire group, but that a variety of types of disordered metabolism might be found in association with focal infection, emotional states and impaired nutrition. Two instances were found which showed an accelerated oxidation which might possibly be termed hyperinsulinism. (Probably these two resemble those described by Ross and Josephs.) Two instances of unexplained relative and absolute diminution in the ability to oxidize sugar without glycosuria occurred. It was thought that one of them was due to hypothyroidism and that the patient could be benefited with thyroid. Others of the group seemed to fit no particular formula. Only six could be studied in detail metabolically.

In a group of thirty-two children, the most common underlying factors distorting the metabolism were the following:

Several of these factors were often present in the same child. Aside from the removal of an underlying cause, a rational basis for frequent feeding and a high carbohydrate diet is confirmed. The use of insulin as a supplement to dextrose has been definitely shown to shorten the duration of the attack by increasing the oxidation of administered dextrose. This treatment probably should not be given in the presence of alkalosis.

FURTHER STUDIES ON ANTIBODIES IN PLACENTAL EXTRACTS. DR. CHARLES F. MCKHANN and DR. FU TANG CHU (by invitation), Boston.

Consideration of the established facts regarding placental transmission of immune bodies to infants and the demonstrable presence in the blood of the umbilical cord of antibodies to diphtheria, scarlet fever and poliomyelitis suggested that placental protein extracts might be prepared which would be capable of increasing the protective reaction of infants to certain disease processes.

We have found that protein material obtained from human placentas by extraction with 2 per cent solution of sodium chloride, concentrated and refined by precipitation with ammonium sulphate, contains substances which (1) neutralize diphtheria toxin, (2) blanch scarlet fever rashes and (3) prevent measles in exposed, susceptible patients. The present studies confirm and extend these observations.

Preliminary tests have shown that the material neutralizes poliomyelitis virus in monkeys. In addition to producing blanching of scarlet fever rashes, the extract has been found to contain an active antistreptolysin. Tests of the material in the prophylaxis of mumps have proved disappointing. The effective material has been found in the pseudoglobulin fraction, precipitated by ammonium sulphate. The euglobulin fraction is small and has been found to lack the antibodies listed.

Placental extract has been administered by intramuscular injection to more than 100 patients. In more than 90 per cent of these patients there was no reaction, local or general, immediate or late, to the injection of the extract.

Further investigation of the preparation, standardization of the product, the determination of the chemical nature and further clinical trials of the preventive and curative value in disease are necessary before the preparation can be suggested for general use.

DISCUSSION

DR. DANIEL C. DARROW, New Haven, Conn.: Some French workers have studied the protein concentration of albumin and globulin in the cord blood and in the blood of the mothers. The albumin has the same concentration in the two bloods, while the globulin is definitely lower in cord blood. Presumably the albumin gets into the infant's blood by diffusion, while globulin may be manufactured or concentrated by the placenta and transferred to infant's blood by some other process. I wonder whether Dr. McKhann has any evidence that extracts of cow's placentas do not have immune substances and that we may, therefore, look on placentas having a special faculty for concentrating globulin in man and in other species.

DR. CHARLES F. MCKHANN, Boston: We have not made studies of the globulins in animal placentas and blood, but I think that the work of Smith and his collaborators, which I mentioned briefly, indicates that these substances are not present, at least in the serum of the new-born animal and presumably in the placenta. Their observations have brought out the lack of globulins in the serum of new-born animals and have drawn attention to the importance of colostrum.

The new-born animal and the new-born infant differ in that the serum of the animal lacks globulin, both pseudoglobulin and euglobulin, whereas the serum of the infant has a normal amount of pseudoglobulin but is lacking in the euglobulin fraction.

POLIOMYELITIS: THE PATHWAY OF INVASION AS DETERMINED BY LOCALIZATION OF THE VIRUS DURING THE PREPARALYTIC PERIOD. DR. HAROLD K. FABER, San Francisco.

With an improved technic for intranasal inoculation of monkeys with poliomyelitis virus, the pathways followed by the virus from the nasal mucosa into and through the central nervous system and the approximate rate of invasion were determined. It was found that about four days were required for the virus to appear in detectable amounts in the central nervous system and then only in the olfactory bulb. By the fifth day it had spread to the hypothalamus and medulla, but was not found elsewhere. On the sixth day it was present in the olfactory

bulb, hypothalamus, thalamus, midbrain and medulla, but not elsewhere in the brain or the spinal cord. On the seventh day it was found for the first time in the spinal cord and spinal ganglions. This rather slow spread by continuity from a definite and sharply localized initial focus along connecting tracts through the brain stem to the cord, with avoidance of contiguous areas in the end-brain and cerebellum, shows that propagation of infection in poliomyelitis is not through the blood or the cerebrospinal fluid, but through the axons of the nerves, as previously demonstrated by Fairbrother and Hurst. Since the route of inoculation used in the experiments corresponds with the natural portal of entry of infection in man, and since the disease produced in the control animals is typical poliomyelitis, the inference is made that the route of invasion found in the monkeys also corresponds with that in man. If this conclusion is correct, the concept of the human disease as consisting of a preliminary stage of systemic, extranervous infection followed by invasion of the central nervous system through a hypothetically damaged "meningo-choroid barrier" is no longer tenable.

The origin of some of the characteristic symptoms at the onset of poliomyelitis in man can, it is believed, be traced to certain areas in the hypothalamus, thalamus and elsewhere in the brain stem which the virus traverses and infects, at least transiently, during its passage toward the spinal cord. A tentative classification of symptoms in chronological order of development is offered, the clinical disease being divided into four successive phases: (1) the cerebral or diencephalic phase; (2) the phase of posterior poliomyelitis; (3) the phase of anterior poliomyelitis; (4) the phase of recovery. The advance of the disease may cease at the end of phase 1 or phase 2, giving rise to the so-called abortive type of poliomyelitis.

THE EVALUATION OF PARENT'S WHOLE BLOOD AS A PROPHYLACTIC MEASURE IN ANTERIOR POLIOMYELITIS. DR. HOWARD CHILDS CARPENTER, DR. JOSEPH STOKES, JR., and DR. IRVING J. WOLMAN (by invitation), Philadelphia.

During the epidemic of poliomyelitis in Philadelphia in the summer of 1932, an effort was made for widespread prophylaxis against the disease by passive immunization. So far as we are aware, such a procedure on a large scale had not been attempted previously.

Six hundred and twenty children under 10 years of age, residing in a carefully investigated census area where the disease incidence was highest, were given intramuscular injections of 60 cc. of parent's whole blood at the Children's Hospital of Philadelphia. Three mild cases of poliomyelitis without paralysis appeared in this group, an incidence of 1 in 207, whereas, according to the statistics of the Bureau of Health, the incidence in the remaining children in the same area and age group during that period was 1 in 640.

Seven hundred and twenty-one children living outside the census area were given similar injections. Three mild cases developed in this group.

In addition, 266 children received from 20 to 40 cc. of parent's serum intramuscularly at the Jewish Hospital; 343 were given 20 cc. of convalescent serum intramuscularly at St. Luke's Hospital, and 229 were given 30 cc. of adult blood subcutaneously at Mount Sinai Hospital. So far as we can determine, none of this number subsequently had poliomyelitis. The ages ranged from 1 to 15 years, although the large majority of the children were under 11 years.

The incidence in this entire number of 2,179 children was 6 cases, or 1 in 363. In the city as a whole, of an estimated population of 289,500 children under 11 years of age, 521 cases of poliomyelitis occurred, an incidence of 1 in 555.

An undetermined number of prophylactic injections of whole blood, adult serum and convalescent poliomyelitis serum were given at other institutions and by many private practitioners. We have been able to collect data on 11 children, who, previous to the attack, had received blood or serum for purposes of passive immunization. Nine of these children had received from 50 to 60 cc. of whole blood from an adult, while 1 had been given 8 cc. and another 15 cc. of convalescent serum. The injections had been given from five to eighteen days prior to the onset of symptoms. In 1 child severe paralysis of both legs developed, in another, moderate

paralysis of one extremity, and in 2 others, slight transient weakness of one extremity. The remainder had no paralysis or weakness, and there were no deaths. Considered as a group, these children had a favorable course in comparison with the rest of the children with this disease in the city, for of the 687 cases in Philadelphia, paralysis developed in about 70 per cent, and the mortality rate was 11.5 per cent.

The blood of the donor for the child who was paralyzed in both legs was found to fail to neutralize a 5 per cent suspension of Philadelphia virus. The other child who was paralyzed received but 8 cc. of pooled convalescent serum.

Although the series of cases is small, we believe that the data suggest that passive immunization by means of adult or convalescent blood or serum is of value as a prophylactic measure against anterior poliomyelitis.

DISCUSSION ON PAPERS BY FABER AND CARPENTER, STOKES AND WOLMAN

DR. JOHN RUHRÄH, Baltimore: I wish to congratulate Dr. Faber on his beautiful demonstration, but I think that it is only fair to call attention to the fact that I missed the point as to the virus he was using. Was he not working with a decided neurotropic virus? The changes he obtained in monkeys are not quite the same as those found in human beings in whom there are definite lesions in the intestinal tract and lymph nodes.

The epidemiology of the disease is more easily explained if it is assumed that something enters into the intestinal tract. I should not say how it gets into the nervous system. Certainly the disease has the general epidemiology of typhoid fever. An enormous percentage of patients have gastro-intestinal symptoms, and there is general enlargement of the lymph nodes.

The epidemiologists in this country have had their attention so firmly fixed on transmission from nose to nose or by carriers that they have overlooked the fact that the disease seems to have some connection with water. What the connection is, I do not know. Possibly there is some relation between the normal spread of virus and the presence of some kind of plant or animal that has to do with water. I think that the point to remember is not only what happens in animals, but what happens under ordinary circumstances.

DR. JEAN MACNAMARA (by invitation), Australia: Dr. Faber's studies carry further the findings of E. W. Hurst and R. W. Fairbrother on the pathogenesis of poliomyelitis after inoculation of a certain strain of virus. Like the English workers, Dr. Faber used the Flexner mixed virus, a strain which has had the opportunity for adaptation of the nerve tissue of the monkey afforded by repeated intracerebral passages over many years.

I think, however, that we should be cautious in assuming that the pathogenesis is identical in poliomyelitis as it occurs in its natural host, the human being.

In yellow fever one does not assume that the path of infection, the selectivity of the virus, is the same in the disease as it is manifested in man on the one hand, and in the white mouse on the other. In the former viscerotropism is evident; in the latter, neurotropism. Recently Herald Cox and Peter K. Olitsky have shown that the virus of vesicular stomatitis, hitherto regarded as epitheliotropic or dermotropic, can become intensely neurotropic in an animal of some other species when inoculated by another route.

While poliomyelitis runs a similar course in man and in monkey after the onset of paralysis, I have been impressed with the difference during the preparalytic stage.

While the monkey has a rise in temperature, ruffled fur and tremor, it does not show acute illness and toxemia comparable to that seen in children. The monkey seems to miss the spine sign stage. Tremor is seen soon after the rise in temperature, and not as the herald of paralysis as it is in human beings.

I regard poliomyelitis in the human being as showing evidence of viscerotropism and neurotropism. In some epidemics one tendency is uppermost. In recent years

in Australia, the viscerotropic phase appears to have increased. In the epidemic in Brisbane in 1931, the general symptoms were so impressive that the dengue state was described by S. F. McDonald.

It may contribute more to our knowledge of poliomyelitis in human beings if studies similar to those of Dr. Faber can be carried out with a strain passed only by the intranasal route from the time of its isolation from the human being and still close to its source, instead of with a virus that has learned to select the nerve tissue of the monkey.

There is evidence that the passage of poliomyelitis virus through a series of monkeys causes it to alter immunologically. The paper Dr. Paul and Dr. Trask presented yesterday threw more light on this problem. Therefore, it seems a wise provision of the workers seeking to learn why certain human serums failed to protect children against the virus of the epidemic in Philadelphia last summer, to decide to test the serum of the donors against a strain isolated during that epidemic and still within a few passages from the human being.

DR. JAMES DOWLING TRASK, New Haven, Conn.: I should like to compliment Dr. Stokes on undertaking studies such as his in the presence of an epidemic. In the stress of the attending circumstances, it is difficult to do the careful work he has done.

I think that the results show plainly how difficult it is going to be to get a definite answer to the problem he has set for himself. One striking thing about the disease which probably makes the answer difficult is its variability. Wickman studied one epidemic in a community of 100 inhabitants; there were 50 cases of poliomyelitis with 11 deaths. In contrast there is the experience of Philadelphia where there was only 1 paralyzed child in 555 cases. I believe that this illustrates the tremendous variation in the disease.

The experience of my colleague, Dr. Paul, and myself showed no sharp line between the abortive form of the disease and the paralytic form. The abortive form affected about 10 per cent of the general child population.

One wonders whether the answer to Dr. Stokes' problem will not have to be sought by the use of the incidence of abortive forms of the disease. Probably, during an epidemic, when the population has been aroused, there have already been many cases of abortive disease in that community.

People say, "How can abortive poliomyelitis be recognized because it is so similar to any minor febrile complaint?" In this connection one sign which we often overlook is the epidemiology of the disease. When an outbreak occurs in a family, most of the members are affected simultaneously. In studying the efficacy of prophylaxis, one could work with the abortive forms of the disease. Instead of having merely 1 case in 550 of the population to work with, one would probably have 50 cases from which to judge the effectiveness of the experimental procedure.

I should like to say that Dr. Stokes' protection test must have been a drastic one if only 5 of 15 of the hospital personnel showed positive protection.

DR. HAROLD K. FABER, San Francisco: In reply to Dr. Ruhräh's remarks, I regret that on account of the shortness of the available time I was unable to consider the various questions he raised. The lesions in man outside of the central nervous system consist essentially of a general lymphoid hyperplasia. With very few exceptions, tests have failed to show the presence of virus in the lymphoid structures excepting in those draining from the nasal mucosa. Clark, Roberts and Preston have shown quite definitely that the monkey cannot be infected by way of the gastro-intestinal tract. The presence of virus in the lymph nodes connected with the nasal mucosa does not contradict the hypothesis of nerve infection, since there is abundant evidence to show that virus is excreted from the brain into the nasopharynx, just as it is carried in the reverse direction to produce infection, and presumably along the same channels.

An analysis of the symptoms at the onset, which also had to be omitted for lack of time, shows that practically all of the symptoms can be explained on the basis of nerve origin. Of the so-called gastro-intestinal symptoms, only one—vomiting—is frequent in all epidemics. This usually occurs suddenly and unexpectedly and

may obviously be due to disturbance of the central nervous system. The subject has been discussed at considerable length in a separate article which has just appeared in *Medicine*.

In reply to Dr. Macnamara's interesting comments, I am fully aware that the MV virus has been trained, but it has been trained to the monkey, and not specifically to nerve tissue, as Dr. Macnamara states. The original human source of this virus was, of course, the tissue of the central nervous system of a child who died of poliomyelitis, and there is no positive evidence that this virus was ever viscerotropic. Even when injected intravenously, its specific effects have always been on the central nervous system, and, so far as I know, the same is true of all specimens of poliomyelitis virus, including those freshly isolated. In the monkey there are certain definite preparalytic symptoms: a rise in temperature on the third or fourth day, apprehensiveness, ataxia, tremor and nervousness preceding paralysis, all of which are perfectly consonant with a nerve infection. In fact, the disease in monkeys is not so different from that in man, save in average severity and tempo, owing possibly to the greater shortness of the nerve paths which permits a more rapid and widespread evolution of the infection.

Dr. Joseph Stokes, Jr., Philadelphia: Dr. Trask has mentioned the severity of our tests for immune bodies in the blood of donors. This has been of considerable advantage in that the donors whose blood showed neutralization of the virus suspension must have possessed a considerable amount of immune bodies. This was true in the parents who apparently protected their children to a certain extent.

We are using a smaller amount of virus for further tests of the blood from the same donors, and shall be able to report later concerning these tests.

As Dr. Macnamara has mentioned, we believe that it was important in our work to use fresh human virus from the Philadelphia epidemic which had undergone only a few passages through monkeys.

NORTH PACIFIC PEDIATRIC SOCIETY

Mid-Winter Meeting, Jan. 28, 1933

Herbert E. Coe, M.D., *President, in the Chair*

Postencephalitic Sequelae. Dr. A. S. McCown, Seattle.

A girl, aged 18 months, was reported on a year ago as having encephalitis. She was a hyperactive child, of normal birth and development, and was walking and talking. She was suddenly taken ill with convulsions and the same evening was sent to the hospital. Clonic convulsive movements were almost continuous; the temperature was 103 F., and lumbar puncture revealed clear fluid under 12 mm. of pressure. The cell count was normal; the sugar content was 68 mg. per hundred cubic centimeters. She was given moderate doses of sodium amytal but received more relief from lumbar punctures. The spinal fluid sugar rose to 83 mg., and the cell count was 8. She was in the hospital from December 5 to December 21. A left external strabismus developed, with muscular weakness on the left side. Throughout the past year there has been gradual improvement. The child sat up about seven months following the illness and took steps three months later. At the present time, at 2½ years of age, she is able to walk alone but walks in a circle, always toward the left. She can say a few words. She is emotionally happy but suffers somewhat from insomnia. Tincture of stramonium, up to 45 minims (2.8 cc.) was administered for the parkinsonian symptoms; calcium gluconate was also used.

DISCUSSION

DR. L. H. SMITH, Portland, Ore.: It is interesting to follow these cases from year to year. I observed a similar case in which encephalitis developed at the age of 7 months. The child on recovery was much like a new-born infant; it began to walk considerably later and looked like an idiot. The prognosis was considered unfavorable. Five and one-half years later the child was not normal mentally.

DR. M. D. SKINNER, Seattle: A child of 9 years, suffering from headache and vomiting, ankle clonus and increased patellar reflexes, could not swallow. A few days later a large quantity of pus and blood, several ounces at least, was discharged through the nose. Paralysis of one side of the face and of the opposite arm and leg developed. Recovery was rather rapid. The original diagnosis was encephalitis; it was changed to abscess of the brain because of the large discharge of pus. Dr. C. F. Eikenbary, who saw the patient later, felt that the orthopedic findings were those of infantile paralysis.

DR. C. U. MOORE, Portland, Ore.: Roughly speaking, the outcome of encephalitis is death in one third of the cases, stigmas in one third and complete recovery in one third. The prognosis must be guarded.

DR. J. T. ABRAHAM, Wenatchee, Wash.: A 13 month old child presented generalized clonic convulsions, with a normal spinal fluid, a temperature of 104 F. and a white blood cell count of 35,000. A blood transfusion was given, and paralysis agitans developed. After a week at a normal level, the temperature again rose to 104 F. The father then revealed that he had been vaccinated ten days previously after an exposure to smallpox. Vaccinia developed in the father, and a few days later in the baby. The temperature dropped to normal with recovery.

DR. H. E. COE, Seattle: Neuromuscular disturbances following encephalitis are helped greatly by muscle training, which should be carried out for from three to six months or longer if necessary.

DR. A. S. MCCOWN, Seattle: I did not give the child in the case reported muscle training.

CHYLOUS ASCITES. DR. A. REMBE, Seattle.

A boy, 20 months of age, was first seen six months ago. Development had been normal. General physical examination gave negative results except for an enlarged abdomen which presented a definite fluid wave ballottement. The child appeared to be perfectly well. There was no fever; the Mantoux test was negative; the white cell count was 6,000, and the urine and blood were normal. Roentgenograms of the abdomen and chest were normal. The abdomen, according to measurement, gradually became larger. Two months ago, 30 cc. of milky fluid was aspirated, which appeared to be chyle. Inoculation of guinea-pigs gave negative results, and laboratory tests of the fluid showed a rather high dextrose content. On the following day intense polyuria developed, and the abdominal enlargement disappeared. It recurred, however, and the abdomen is now as large as ever. In the differential diagnosis, tuberculous peritonitis was considered, as well as chylous cyst and chylous ascites due to obstruction. Tuberculous peritonitis was ruled out, and the diagnosis of chylous cyst is favored. As the only air-containing space has always existed well back in the flanks and the intestines and stomach were always displaced backward even when the child was lying on his back, the explanation of the polyuria and the disappearance of the tumor is that following paracentesis the fluid leaked into the abdominal cavity and was absorbed and excreted through the kidneys. In all probability there is no malignant obstruction of the thoracic duct, as it should be palpable by this time.

DISCUSSION

DR. W. F. PATRICK, Portland, Ore.: Has a barium sulphate meal been used? This should show displacement of the bowel and stomach.

DR. N. W. CLEIN, Seattle: Have diuretics been used?

DR. E. J. BARNETT, Spokane, Wash.: What relief might be obtained from diuretics? The aspiration of large amounts of fluid is, in my opinion, inadvisable, and I question the advisability of emptying the cyst at operation.

DR. N. W. CLEIN, Seattle: Novasurol might be of benefit, and one or two further aspirations might be tried.

DR. H. E. COE, Seattle: I consider the case one for surgical intervention. I contemplated partial aspiration before operation but felt that the cyst probably connected with the intestinal lacteals and not with the thoracic duct, probably being a mesenteric chylous cyst.

DR. A. REMBE, Seattle: But for the presence of respiratory infection the child would have been operated on this week. He will be sent home and returned for operation, and the case will be reported at the next meeting.

MORQUIO'S DISEASE. DR. E. J. BARNETT, Spokane, Wash.

This condition, which consisted of severe osseous dystrophy, occurred in two sisters. The paper will be published in full, with illustrations, at an early date.

HEMOLYTIC PURPURA AND HEMOLYTIC JAUNDICE. DR. A. H. SPOHN, Vancouver, B. C.

DISCUSSION

DR. E. J. BARNETT, Spokane, Wash.: In a child 3 months old, in whom the bleeding time was greatly prolonged and no platelets were found, all treatment, including transfusions, was of no avail. Splenectomy was finally resorted to. On the following day the bleeding time was four minutes. There were 74,000 platelets. Bleeding ceased. A week later the bleeding started again, and the platelet count had been reduced to 4,000. A question as to the possibility of an accessory spleen arose.

OCULAR TORTICOLLIS. DR. A. E. WADE, Seattle.

In many cases in which operation for torticollis is performed, the condition is undoubtedly of the ocular type. A child, 12 years of age, had tonsillitis three years ago which was followed by double vision. This attracted little attention, but a short time later she was brought to the hospital because of torticollis. When the head was straightened, the left eye turned upward, showing paralysis of the left superior oblique muscle. Dr. Bentley, who was consulted regarding the ocular condition, advised no operative treatment at that time. The improvement in this case has been gradual, but recovery is not complete, and probably operation will have to be performed.

ACUTE ABDOMEN IN CHILDREN. DR. D. H. HOUSTON, Seattle.

A girl, 5 years of age, was admitted to the hospital on Dec. 7, 1932, with acute vaginitis acquired through sleeping in the same bed with her father, who was suffering from an acute flare-up of an old urethritis. Vaginal smears showed abundant gonorrheal organisms. There were no symptoms other than those of acute vaginitis, and the temperature was normal during the first five days in the hospital.

At 10 p. m., on December 11, the child complained abruptly of severe generalized abdominal cramps. She was given codeine sulphate, ¼ grain (0.015 Gm.), at 3 a. m. by the resident physician, with only slight relief, and at 5 a. m. she vomited. By 8 a. m. the temperature was 103 F., and the pulse rate, 130; the child was still very uncomfortable, with general abdominal pain, and there was definite tenderness over the lower part of the abdomen, more marked on the right side. The leukocyte count was 37,900. Since the child was in the hospital solely for the treatment of gonorrheal vaginitis, the natural deduction was that she suffered

now from an ascending infection, with resultant acute salpingitis and peritonitis. She was examined several times during the day; the tenderness over the lower part of the abdomen, with maximum intensity over McBurney's point, persisted. Rectal examination disclosed tenderness to the finger-tip but no abnormal fulness. The sedimentation of the blood cells from the plasma was abnormally rapid.

The point of decision in the differential diagnosis was reached at 4 p. m., on December 12, eighteen hours after the onset of the attack, when the temperature fell to 99.6 F. and the pulse rate to 110, with persistence of the pain and tenderness in the lower part of the abdomen and a leukocyte count of 39,000. A diagnosis of acute appendicitis was made. An additional factor in favor of this diagnosis was the fact that despite the severe pain and tenderness in the lower part of the abdomen the patient did not have the toxic facies usually seen with pelvic peritonitis sufficiently severe to cause the sudden elevation of temperature and the leukocyte reaction present in this case.

At 5 p. m., the abdomen was opened through a lower right rectus incision. The appendix was acutely inflamed, with generalized injection of the peritoneum. The uterus, tubes and ovaries were normal. The appendix was removed. The convalescence was uneventful, the patient leaving the hospital on January 14, after the vaginitis had subsided and smears were repeatedly negative.

In an abdomen presenting an acute surgical condition it is not necessary to delay for an accurate diagnosis. It is better to have a living patient than an accurate diagnosis. In a recent case my associates and I contested with consultants as to whether a suddenly tender abdomen and other symptoms in a child were due to acute appendicitis or to intestinal intussusception; all, however, agreed that the condition of the abdomen required immediate surgical intervention. Operation was performed at once, and an intussusception was found at the ileocecal valve, caused by a Meckel diverticulum. It was reduced before it reached the point of strangulation, and convalescence was smooth. Had too much time been taken in deciding between two surgical conditions, the child's life might have been lost.

However, in the case presented here, guarded delay was justified, for the question lay between two conditions, the one urgently surgical, the other distinctly nonsurgical. In such cases the classic symptoms of an inflamed appendix and the atypical variations cannot be reviewed too carefully. An important aid in the diagnosis in this case was the rather universal experience that gonorrhea, probably because of the anatomy of the child's genital tract, usually remains in the vagina and urethra and rarely ascends to the tubes.

Had salpingitis been found at operation, we should have closed the abdomen without removing the tubes.

SOME PHASES OF ACUTE ABDOMINAL CONDITIONS IN INFANTS. DR. W. B. SEELYE, Seattle.

The following cases have been chosen as representative of some of the different types of intestinal obstruction seen in both hospital and private practice. Each is distinctive in one or more features, and each presents points unusual enough to stimulate one's diagnostic abilities.

CASE 1.—J. T. was one of twins born prematurely at six and one-half months, by spontaneous delivery in breech presentation, on Sept. 4, 1932, at Harborview Hospital. She was a small, essentially normal but immature infant, weighing 3 pounds and 2 ounces (1,417.48 Gm.) at birth. Insufficient mother's milk was supplemented by an evaporated milk, water and sugar formula, and the baby was kept in a heated bed. On the seventh day the temperature rose to 102 F. (rectal), and for the succeeding nine days it fluctuated between 99 and 102.6 F. From this time on, the baby remained afebrile, but vomiting set in, together with a persistent and intractable diarrhea. Abdominal distention was noted at times, but this was easily relieved by enemas. At no time was there tenderness, visible peristalsis, muscular rigidity or palpable masses. Rectal examination gave negative results. The chest was clear, and there were no reflex disturbances, Kernig

sign or rigidity of the neck. Gavage was instituted, and finally parenteral fluids were given daily as the vomiting became more and more pronounced. Blood transfusion was ordered, but death supervened before this could be done. Postmortem examination revealed: ileocecal obstruction (intussusception); hemorrhagic necrosis (impending gangrene); acute generalized fibrinopurulent peritonitis, and marked distention of the small intestine. This was a clearcut case of intussusception without any of the classic symptoms except vomiting; there was no mucus or blood in the stools at any time, and no tumor mass was palpable in the abdomen.

CASE 2.—J. T., the twin sister of the patient in the first case, weighed but 2 pounds and 8 ounces (1,133.98 Gm.) at birth. Delivery was normal. On breast milk and various supplementary formulas, the weight was brought up to 4 pounds (1,814.37 Gm.) on the thirty-third day of life. Regurgitation was first noted on the nurse's chart on the first day of life. As many as nine loose stools per day were recorded intermittently; these contained no blood or mucus and were bile-stained. The vomiting was persistent but never projectile and was not associated with fever. Toward the last, the weight was kept up by parenteral administration of fluids. The baby died without showing at any time any of the accepted signs of an acute abdominal pathologic condition. At postmortem examination, numerous congenital adhesions and bands were found about the cecum, with evidence of partial intestinal obstruction. No signs of acute peritoneal inflammation were noted.

CASE 3.—D. J. M., a girl, born at full term, was normal until two weeks before admission to the Children's Orthopedic Hospital, when, at the age of 7 months, she began to vomit occasional feedings. At the end of the first week, the vomiting became projectile, and the stools and urine diminished in volume. During this time the parents were said to have noted "very marked, gurgling, visible peristalsis all over the abdomen." There was no blood or mucus in the stool. No relief resulted from the administration of atropine. For two days prior to admission, the vomiting had been fecal. There were moderate abdominal distention and marked dehydration. Examination of the urine showed 1 plus albumin, with an occasional epithelial cell in the sediment. A diagnosis of intestinal obstruction was made, and operation was advised.

At operation the small bowel was found to be markedly distended, and there was a hard, cystic tumor at the ileocecal valve, about 1½ inches (4 cm.) in diameter, completely blocking the opening, arising apparently from a mucous gland and distending the intestinal wall beneath fibrous and muscular portions of the ileocecal valve from the mesenteric border about one half of the circumference of the ileocecal valve. The appendix was not involved. There were no bands or adhesions. The cyst contained clear, uninfected mucus. Its walls were about ¼ inch (0.6 cm.) thick and fibrous. The bowel could be invaginated through the ileocecal opening after the cyst was opened, its lumen being slightly larger than the index finger. Tissues overlying the cyst were pale and bloodless from pressure. A large amount of clear fluid was found free in the peritoneal cavity. After an attempt to shell out the tumor through an incision in the serosa had failed, an enterostomy opening was made into the ileum and a catheter was placed in the intestine. The cyst was then opened, and sections were removed for biopsy, the remaining portions being everted up into the wound and the interior surfaces left exposed to the peritoneal cavity. Postoperative recovery and convalescence were uneventful.

CASE 4.—R. S. was admitted to the Children's Orthopedic Hospital at the age of 9 months because of persistent projectile vomiting since birth. The patient was one of twins; the brother was said to be normal in every respect, weighing 20 pounds (9,071.84 Gm.). Peristaltic waves had been seen by the attending physician and by the parents. Thickened feedings, atropine, phenobarbital and various formulas had been tried with indifferent success, the vomiting continuing in spite of all measures to control it.

Examination at the time of admission to the hospital showed an emaciated, poorly nourished male infant, weighing but 10 pounds and 12 ounces (4,876.12 Gm.).

The head was slightly squared and was disproportionately large, with prominent eyes. The facies was pinched and narrow. The anterior fontanel was 2.5 cm. in diameter, soft and level. The ears, eyes, nose, mouth and pharynx were normal. There were no teeth. The chest was thin, clear and resonant throughout. The heart was normal. The abdomen was thin and sunken, with some muscular rigidity. No masses were seen or felt, and there was no visible peristalsis. The liver, spleen and kidneys were not felt. The genitals were normal. The extremities were extremely flaccid and thin. The general skin and muscle tone was poor. Fluoroscopic and roentgen examination showed a well outlined stomach with considerable retention of an opaque meal at the end of two hours and less retention at four hours; the stomach was empty at six hours. The diagnosis was partial intestinal obstruction due to a band or bands of congenital origin, and operation was advised.

Prior to operation 300 cc. of physiologic solution of sodium chloride was given subcutaneously; this was followed by a sharp rise in temperature, which had been normal, to 104 F. (rectal). The patient was given a diet of an evaporated milk, water and dextrimaltose formula with thick cereal added, which he retained but did not take well. The following day 150 cc. of a 10 per cent dextrose solution was given intravenously, following which the temperature returned to normal. At operation the stomach was found to be large, with abnormal fixations in the region of the pylorus. Its blood supply was normal. The pylorus was not abnormally thickened or enlarged. There was a band 1.5 cm. wide running from the under-surface of the liver downward and medialward to an attachment at the juncture of the first and second portions of the duodenum. The duodenum was abnormally free and mobile. The upper portion of this band was cut and tied off down to a colorless duct about 2 mm. in diameter. This relieved somewhat, though incompletely, the tension of the duodenum; there was less acute angulation of the bowel after this had been done. The postoperative course was stormy from the first day, and death occurred on the eighth postoperative day as a result of diffuse bronchopneumonia. At postmortem examination the abdominal findings were verified; there were an extensive bronchopneumonia and a moderate degree of internal hydrocephalus. The presence of the internal hydrocephalus emphasizes the fact that when one congenital defect is found, others should be looked for and often are found.

Case 5.—H., a boy born at term, by uneventful breech delivery, was the first baby of healthy, young parents. The Wassermann test of the blood was negative in both the father and the mother. During pregnancy the mother was known to have had influenza; otherwise the pregnancy was uneventful. At birth the baby seemed lifeless and hard to arouse, with shallow respiration, poor color and weak pulse. Feeding was troublesome from the start. Breast milk was alternated with various formulas in attempts to find a food that would agree with the infant. The weight at birth was 5 pounds and 14 ounces (2,664.86 Gm.), and at 2 weeks, 6 pounds (2,727.55 Gm.). At this time the baby was sent home from the hospital, where things went from bad to worse, culminating in the fourth week in a series of convulsions. The patient was readmitted to the hospital in a very weak condition. The weight dropped steadily to 5 pounds and 6 ounces (2,438.26 Gm.). I first saw the child at the age of 6 weeks, because of failure to gain weight. The convulsions had not recurred. There was a profuse nasal discharge, and the right nostril was badly excoriated. On the buttocks a large area of superficial ulceration had developed around the anus. The bowels were loose, and movements were frequent. Examination at this time showed a sickly, pale, weak, emaciated male infant, with a weak, pitiful cry. The bony structures were fairly normal, but the skin was flabby and the muscle tone poor. The lower extremities were slightly flaccid; the upper extremities slightly spastic. The breathing was cogwheel in type, with an expiratory grunt. There were bronchovesicular breath sounds throughout the entire left side of the chest anteriorly and into the axilla, with fine, crepitant râles. Resonance was not impaired. The heart was not enlarged to percussion, and its rate and rhythm were normal. No murmurs were

heard. Both testes lay high in the inguinal canals, and there was an easily reducible inguinal hernia on the right side.

Because of the history of convulsions and slight but definite spasticity, a spinal puncture was done. Twelve cubic centimeters of clear fluid was withdrawn, which was under very slightly increased pressure. The laboratory reported 40 cells, all lymphocytes, 60 mg. of sugar, 1 plus globulin and no organisms on smear or culture. Several days later the Wassermann test was reported as negative. The baby's condition grew steadily worse, and death occurred within a few hours.

Autopsy Report: When the abdomen was opened, there were numerous adhesions between the loops of bowel, the intestinal wall, the omentum and various organs, giving the impression of an intra-uterine peritonitis which had healed. There was rather marked enlargement of the liver, which was very dark. The liver was attached to the spleen with a definite fibrous tissue structure. The spleen was small, about 1½ inches (4 cm.) long. The pancreas, gallbladder and stomach appeared normal. The left kidney was about normal in size and shape and was lobulated. The right kidney was made up of a few cystic masses, practically no renal tissue being present. The right lung contained three regular lobes, and there was a fourth present on the lower anterior surface of the upper lobe. The head was opened. A large amount of fluid exuded from the brain. When the cortex was opened it was found that each lateral ventricle made up about two thirds of the cranial volume. A calcified nodule was present at the base of each choroid plexus. Section through the metaphyseal line of the elbow showed the osteochondral junction to be a straight line. There was no evidence of congenital syphilis. The lungs showed bronchopneumonia.

The anatomic diagnosis was: congenital hydrocephalus; congenital absence of the right kidney; congenital accessory lobe of the right lung; congenital adhesions of the abdomen; congenital union of the spleen and liver, and terminal bronchopneumonia.

I shall omit, because of lack of time, discussion of any of these conditions except that in which the members of the society are most interested at this moment, namely, fetal or intra-uterine peritonitis. In reviewing the literature, one is struck by several outstanding facts. In the first place, until recent times this condition was thought always to be due either to syphilis or to tuberculosis. A case was reported by Manclaire and Alglave in 1900 in which tuberculous peritonitis was discovered at autopsy in an infant who lived six days. "At necropsy there were several strictures of the intestine and tubercle bacilli were demonstrated in the enlarged mesenteric glands, with giant cells in the tuberculous areas in the intestinal wall." One of the best reviews and discussions of fetal peritonitis is found in I. A. Abt's article in the *Medical Clinics of North America* (**15**:611, 1931).

The data on one of the cases reported were furnished by Dr. H. E. Coe. Two cases are from my private practice, and two from the pediatric service at Harborview Hospital.

DISCUSSION ON PAPERS BY DR. HOUSTON AND DR. SEELYE

Dr. H. E. Coe, Seattle: In case 3, an obviously acute abdominal condition grew progressively worse. Operation was finally performed and revealed a submucous cyst, causing obstruction of ball valve type. The time of operation is important; one should always get the child into the best condition possible and should not delay for a too finely drawn diagnosis. Infrequently one must consider the coexistence of two conditions. Peritonitis in small children is not easily diagnosed.

Dr. C. L. Smith, Seattle: I observed a case of peritonitis in a child 5 days old. The temperature was 100.6 F. The patient vomited from the first feeding. Roentgen examination showed some bismuth throughout the intestine and also demonstrated a dilated esophagus which filled before any barium sulphate entered the stomach. The barium was apparently vomited from the esophagus, although roentgen study demonstrated retention for twenty-four hours in the stomach. The

child was cyanosed occasionally. No diaphragmatic hernia existed. The patient finally recovered.

DR. W. F. PATRICK, Portland, Ore.: I observed two cases of dilated esophagus in children, one with a pouch and one with a double esophagus, one branch connecting with the intestinal tract. Both patients died.

DR. J. T. ABRAHAM, Wenatchee, Wash.: A 19 month old child presented a typical case of intussusception. Operation was performed, and the condition was reduced satisfactorily. Twelve hours later the vomiting started again. Colostomy was done, and a second intussusception was found, which probably existed at the time of the first operation. In some cases, moreover, intussusception may occur post mortem or terminally.

DR. C. U. MOORE, Portland, Ore.: What evidence is there that meconium may carry infection into the peritoneal tract before birth, which would be from eight to twenty hours before the contents of the bowel become infectious?

DR. W. B. SEELYE, Seattle: Meconium is probably not infectious, and severe vomiting during the first three days of life indicates probable intestinal obstruction.

DIFFUSE NEPHRITIS. DR. C. L. SMITH, Seattle.

A boy, 12 years old, was admitted to the hospital on Nov. 11, 1932. He had had a respiratory infection one week previously, with edema of the face. Seven days after admission, coma developed. The skin was flushed, with livid spots and there was considerable edema of the face. The blood pressure was 148 systolic and 92 diastolic, and the breath was definitely urinary. There was a systolic murmur at the apex. The reflexes were hyperactive. There was anuria during the next twenty-four hours. The first specimen of urine examined contained albumin, 4 plus, occasional pus cells and red cells, 20 to 30 per field. The blood urea was 32.4 mg. per hundred cubic centimeters, creatinine 7.5 mg., and cholesterol 64 mg. The hemoglobin was 62 per cent; the red blood cells numbered 3,300,000. One fluidounce (30 cc.) of magnesium sulphate was given by stomach tube every four hours, and 600 cc. of 5 per cent dextrose in saline solution was administered intravenously. Morphine, 1/6 grain (0.01 Gm.), was given hypodermically for convulsions. Three grains (0.18 Gm.) of sodium acetate (theocin) was given three times daily. The coma was intermittent, with delirium, during the next twenty-four hours. After this liquids were taken by mouth, and at the end of the second day he began to void. Nonprotein nitrogen was 96.3 mg. per hundred cubic centimeters; urea 45 mg., and creatinine 2.5 mg. On the third day the patient was rational but complained of headache. The blood pressure was 162 systolic and 92 diastolic. Potassium citrate, 10 grains (0.6 Gm.), was given every four hours. The edema seemed to be increasing, and also the diplopia. Ophthalmic examination showed blurred disks. On the sixth day the blood pressure was 131 systolic and 84 diastolic. One month later the urine showed albumin, 1 plus, and 3 red cells per field. The blood urea was 16.2 mg.; creatinine, 0.5 mg., and nonprotein nitrogen, 34.6 mg. Roentgen examination of the sinuses showed the right frontal sinus and also the antrums to be slightly cloudy. The child was discharged on December 31, with the urine showing albumin, 1 plus, and no red cells. On January 27 a cold developed, with no increase in the edema and no ocular symptoms. The blood pressure was 104 systolic and 48 diastolic; the urine was free from albumin; the hemoglobin was 70 per cent, and the red blood cells numbered 4,000,000. Dr. Smith felt that the child would have died twenty-four hours later had not active treatment been instituted. According to Aldrich, magnesium sulphate does not result in catharsis even when given in fairly large doses in the presence of edema. The action of sodium acetate (theocin) is enhanced by potassium citrate.

NEPHRITIS. DR. V. W. SPICKARD, Seattle.

The patient was admitted to the hospital on Aug. 18, 1932. The past history was unimportant until nine months previously, in November, 1931, when puffiness

developed under the eyes and the urine contained albumin, casts and red blood cells. In April, 1932, a similar attack, but not so severe, occurred. In July, 1932, the present illness started. On examination, the child weighed 47 pounds (21.3 Kg.); the temperature was normal; there was slight puffiness under the eyes; the cervical glands were palpable, and the thyroid gland was slightly enlarged. The tonsils and adenoids had been removed. The cardiac area was elevated two finger-breaths outside the nipple line. There were slight clubbing of the fingers and pitting of the extremities. After two days in bed the edema disappeared, but it recurred later. The antrums and the left mastoid sinus were cloudy. The sinuses were irrigated, and pus was obtained. After the administration of novasurol the child lost 3 pounds (1.4 Kg.). The nonprotein nitrogen of the blood was 36.4 mg. per hundred cubic centimeters; urea, 17.4 mg.; creatinine, 0.2 mg., and cholesterol, 200 mg. On August 25, the nonprotein nitrogen was 27.2 mg. The administration of 6 grains (0.36 Gm.) of thyroid extract was followed by no improvement. Magnesium sulphate was given, with no result. Two grains (0.12 Gm.) of theophylline three times daily, alternating or together with potassium citrate, was given until Dec. 7, 1932. The weight was then 52 pounds (23.6 Kg.), and there appeared to be no edema. In October, 1932, lymphangitis of the legs developed. On Jan. 9, 1933, following respiratory infection, there was no exacerbation of the symptoms. A specimen of urine was practically normal.

NEPHRITIS. DR. J. J. DURAND, Seattle.

CASE 1.—A boy, 8 years old, who but for occasional mild tonsillitis had been perfectly healthy, had a series of boils between July 4 and September 1. A small abscess developed over the knee, and on September 20 the child began to pass bloody urine. The blood pressure was 110 systolic and 65 diastolic with the onset of edema. He was put to bed, and magnesium sulphate was administered. The tonsils at this time became acutely inflamed. Three days later, while the patient was still in bed, the condition of the urine had not improved and the blood pressure had risen to 142 systolic and 110 diastolic. The edema of the face had become marked. Nonprotein nitrogen was 36 mg. per hundred cubic centimeters, urea 16 mg., and creatinine 0.3 mg. Dr. Miller, who saw the child in consultation, agreed that the tonsils were probably at the base of his troubles and advised removal as being a lesser hazard than the rising blood pressure and increasing renal damage. Under ether anesthesia, the tonsils were removed with no apparent exacerbation of the renal disturbance. On September 26, the urine showed from 80 to 100 red cells in each high power field. The albumin began to diminish and one week later there was only a trace, with an occasional hyaline cast. The boy then had fever for two days, with an increase in albumin and casts. From then on the urinary improvement was steady. Two weeks later there was a further trace of albumin, with some hyaline casts. Again there was an exacerbation, at which time the blood pressure was 130 systolic and 90 diastolic; it then dropped to 126 systolic and 80 diastolic. A few weeks later the blood pressure had dropped to 110 systolic and 80 diastolic. Both the blood pressure and the urine have remained normal ever since.

CASE 2.—The condition on which I shall report is not unheard of in adults but is rarely found in children. A girl 14½ years of age had been seen once a year throughout childhood. On the last examination the urinary albumin had been 2 plus. In the fall of 1932 she came to my office in a serious condition, with the albumin boiling solid in the urine. Hospitalization was advised. As the mother was ill, the advice was not followed. Three months later the child began to vomit, complained of headaches and double vision and had lost 12 pounds (5.4 Kg.). The blood pressure on office examination was 280 systolic and 175 diastolic; this was verified by Dr. Spickard. There were albumin and casts in the urine but no red cells. Twenty-four hours later the blood pressure was 245 systolic and 180 diastolic. The heart rate was rapid. The white blood cell count was 6,000, with a normal differential count. The urine showed albumin, 4 plus; no sugar; many hyaline and

granular casts, and a few red cells. The Wassermann reaction of the blood was negative; the nonprotein nitrogen was 45 mg. per hundred cubic centimeters, and the creatinine, 2 mg. The excretion of phenolsulphonphthalein was 15 per cent the first hour and 15 per cent the second hour. The spinal fluid was under 30 mm. of pressure, and the sugar content was 83 mg. per hundred cubic centimeters. The diagnosis was essential hypertension. A month later the child died. Postmortem examination showed terrific disease of the arteries; the lumens were almost occluded, and the walls were like pipe stems. The lungs were almost solid; the kidneys were hemorrhagic and necrotic. Dr. Keith at the Mayo Clinic has described such a condition as malignant hypertension.

DISCUSSION ON PAPERS BY DR. SMITH, DR. SPICKARD AND DR. DURAND

Dr. Armin Rembe, Seattle: Does the family history in Dr. Durand's second case contain evidence of hypertension or other significant information? I observed a case of scarlet fever with puffiness but no pitting. Ten days after the temperature became normal the urine was bloody. The systolic blood pressure was 115. The blood chemistry was normal; there were choked disks. There was evident retention of fluid, as well as edema of the brain. Hypertonic dextrose solution was given intravenously, and magnesium sulphate by mouth. There was complete clinical recovery.

Dr. N. W. Clein, Seattle: I observed a case in which a child who had been operated on for mastoiditis a month before returned to the hospital with dyspnea and infrasternal and substernal retraction. There was a question as to the cause of the difficult breathing. Diphtheria antitoxin was given and bronchoscopy was done. No membrane was seen, but only a diffuse bronchitis. Coma supervened. The child was intubated, with no relief. Eighteen hours later he died. Postmortem examination showed two contracted, white kidneys. This case illustrates the difficulties that arise in differential diagnosis.

Dr. L. H. Smith, Portland, Ore.: In regard to Dr. Durand's first case, I do not feel that the high blood pressure was a contraindication to removal of the tonsils during the acute process, since there was no fever.

Dr. W. F. Patrick, Portland, Ore.: In a case of acute nephritis, with blood and albumin in the urine and with fever, the tonsils were removed and the patient recovered.

Dr. A. H. Spohn, Vancouver, B. C.: I observed a case in which the tonsils and adenoids were removed by an otolaryngologist on the recommendation of a pediatrician a month after a rheumatic attack. There was no fever, and the heart was normal. Immediately following the operation fever and endocarditis developed, and the child died. There were medicolegal complications.

Dr. J. T. Abraham, Wenatchee, Wash.: I think that the tonsils may be removed in any stage of nephritis.

Dr. C. L. Smith, Seattle: Chronic nephritis should give one a great deal more worry than the acute type. The basis is a recurrent or chronic infection.

Dr. J. J. Durand, Seattle: It is significant that the question of diet has not entered this discussion; a few years ago it would have dominated the discussion.

Pathologic Conditions of the Kidneys. Dr. R. E. Mosiman, Seattle.

Case 1.—A girl, 12 years of age, three years prior to examination had dyspnea, edema and dysuria with bloody urine, which lasted four weeks. She was well until five days before examination, when the urine became bloody with albumin 4 plus, the temperature fluctuated from 97 to 102 F., and the blood pressure was 142 systolic and 130 diastolic. The heart became enlarged, and the blood pressure rose to 156 systolic and 126 diastolic. Cardiac paracentesis was done. Only blood was obtained, with creatinine 5.8 mg. per hundred cubic centimeters. Post-

mortem examination showed that the kidneys contained old scarring, demonstrating that clinical recovery was only apparent.

CASE 2.—A child, 10 years old, lost weight and had dull pain in the left side. There was frequency of urination. Albumin 1 plus was found. A perinephritic abscess developed. This was drained, and later the kidney was removed.

CASE 3.—A boy, 11 years old, in jumping from the porch had fractured his elbow. Shortly afterward pain developed in the left side, and the urine was bloody. Chills, nausea and vomiting occurred. Edema developed over the injured elbow; the pus was aspirated but was negative on culture. Cystoscopy showed that the right kidney was normal, but that there was no urinary flow from the left kidney. Urine from the right kidney was negative on culture; that from the left showed Staphylococcus. There was hydronephrosis of the left kidney. The left kidney was removed.

CASE 4.—In a child recovering from scarlet fever swelling of the left leg developed. There were acute shock, sweating, and pain on the left side. Cystoscopy showed no secretion of urine from the left kidney. A diagnosis of infarction was made. Anuria developed, and at autopsy thrombosis of the vena cava was found.

CIRCUMCISION. DR. F. H. DOUGLASS, Seattle.

Evidently the operative procedure known as circumcision is considered by medical authors as too insignificant to demand much attention for there is little material in the literature on why, when and how the procedure should be done. I am sure that if an operation of equal size were to be carried out on the face there would be many ideas, and certainly the work would be more carefully done.

I wish to present some ideas on circumcision in male infants and children. In the first place, I firmly believe that "anything worth doing is worth doing well," and after observing the results of the operation as performed by many physicians, I am certain that the operation is not generally done well. Perhaps the reason for this is that many doctors consider the procedure too unimportant to perform, and they leave it to an intern without first teaching him a technic.

There should be a reason for performing any operation. There should be indications and contraindications. I do not feel that all boys should be circumcised, but they should be examined to see whether the operation is indicated. In all new-born boys there is a certain amount of phimosis, which varies greatly in degree and should receive attention. Often little treatment is needed, and the phimosis can be relieved by stretching. Each day the prepuce should be retracted a little farther until the phimosis is completely relieved and the glans may be exposed. If this can be accomplished within the first ten days or two weeks circumcision is not indicated.

Indications for Circumcision.—1. Phimosis: This is such a narrowing of the prepuce that it cannot be retracted. When phimosis is present, cleanliness is usually impossible; this frequently leads to balanitis, sometimes complicated by urethritis or even by cystitis.

2. *Redundant Prepuce:* Frequently one sees a long, excessive prepuce, either with or without phimosis. This condition does not allow for the free elimination of urine from the urethral meatus. The urine must flow through this redundant tissue, which, because of its folds, does not drain well. The retention of drops of urine produces irritation and acts as a medium for infection, frequently resulting in balanitis.

3. *Adherent Prepuce:* Most frequently associated with phimosis, redundant prepuce or both, but also found alone, is adherent prepuce, the condition in which the mucous membrane is adherent or grown tight to the glans penis. This is due to failure to retract the prepuce and leads to the accumulation of smegma in pockets about the corona. This is a source of severe irritation and uncleanliness.

Physiology of the Part.—The glans is the most sensitive part of the penis, and the corona, the most sensitive part of the glans. It is therefore important that

there be enough prepuce to cover the corona, but that it be short enough to leave the urethral meatus free and wide enough to allow for easy retraction. The mucous membrane, which is frequently excessive, presents a secreting surface which may become adherent and form pockets filled with smegma. In this case it is necessary to remove this tissue, replacing it with inverted skin from the prepuce. In cases in which there has been adherence of the prepuce to the glans, especially when there has been an associated balanitis, there are formed adhesions of the areolar tissue between the mucous membrane and skin which act as a further irritation to the part. This point is frequently overlooked in circumcision.

Time for the Operation.—The baby should be operated on during the first six weeks, preferably as soon as he regains his birth weight, or else the procedure should be postponed until he is over a year old, is not fed from a bottle, has a rather stable diet and is past the diaper stage. Unless there are definite indications it is best not to circumcise a new-born infant, but to wait until he has been at least partly trained, as the prepuce acts as a protection to the wet meatus. One frequently sees excoriated meatuses as well as meatal ulcers in circumcised infants owing to rubbing of the wet meatus on the diapers or of the wet diapers on the meatus. This condition is rare in uncircumcised children.

Preparation of the Infant.—Infants up to 5 or 6 weeks of age need no anesthetic other than a gauze sponge soaked in sugar syrup containing 10 drops of whisky. This usually satisfies the infant, but it is necessary to restrain him. For this, a padded Y frame is used, and the patient is held firmly to the frame with towels, one about his waist and the body of the frame and another over each knee and about the corresponding arm of the frame. The binders should be firm enough to immobilize the infant, but should in no way act as constrictors. For older children no frame is needed, and ether is the anesthetic of choice.

Preparation of the Part.—The penis, prepuce and pubes are thoroughly cleansed with tincture of green soap. This is removed with sterile water, and the area is dried with gauze. Then the constriction is dilated, adhesions are broken up, the smegma is removed, and the application of green soap and water is repeated. The area is dried, and 70 per cent alcohol is applied. Care should be taken not to allow any of the fluids to run down over the perineum. Next, the mesh of a sterile gauze sponge is separated with a hemostat until the opening is sufficient and the penis is put through this perforation. When the mesh is separated, with a blunt, dull instrument there are no fragments or threads to encumber the field. Draping is completed with sterile towels. Gloves may be worn if desired, but a strictly aseptic technic should be employed, and it must be remembered that "a clean glove has never covered a dirty hand."

Technic of the Operation.—The prepuce is retracted, completely exposing the glans, and after the folds are separated, the constricting band is isolated. At the junction of the constriction with the median raphe on the ventral surface, a mosquito hemostat is placed, and another is placed on the dorsum, also holding the constricting band. With the clamps held by the operator, the prepuce is again pulled over the glans, and a pair of thumb forceps is applied proximal to the instruments on an angle parallel to the corona. One should be sure that the median raphe is in the midline. The amount of tissue to be removed varies in each case; when this is estimated and the clamp is in place, an incision is made proximal to the forceps. This removes the constricting band and leaves the cut parallel to the corona. At this time hemorrhage should be controlled. For this purpose, I use sponges wet with hot boric acid solution and plain 00 catgut for ties. When hemostasis is complete, two mosquito forceps are placed on the dorsum of the cut edge of the mucous membrane, and the tissue between the instruments is separated down to within about 3/16 inch (0.5 mg.) of the corona. The mucous membrane on each side is now held between the thumb and first finger, and with scissors cutting down on the first finger, which is under the tissue, the membrane is cut about the corona, 3/16 inch peripherally to it; adhesions of the

areolar tissue are made free, and the mucous membrane is removed. All the dissection is done with scissors. This removes the secreting surface and obviates the possibility of recurring adhesions and redundancy. Any remaining bleeding vessels are now controlled before suturing. The first stitch is taken at the frenum, where a mattress stitch is used. The stitches are taken beginning on one side of the raphe, the needle being passed through the skin and then through the mucous membrane over the frenum and then brought back on the opposite side of the raphe. With a mosquito forcep the cut end of the frenum is tucked in and the stitch is closed in a purse-string manner. After the knot is tied, the ends are cut short. The edges of the cut skin and mucous membrane are approximated at the dorsum, and whatever stitches are necessary are taken on each side. Frequently four sutures are all that are needed, and it is best to suture from the mucous membrane to the skin in order to eliminate the possibility of tearing. Sterile boric acid ointment is applied about the suture line, and the drapes are removed down to the gauze surrounding the shaft of the penis. With the index and middle fingers of both hands under the gauze, supporting the penis, and the thumbs on the meatus, the gauze is removed and at the same time the suture line is inverted and the skin is pulled up over the corona. For dressing, a 4 by 6 inch (10 by 15 cm.) gauze sponge split like a pair of trousers straddling the penis with the body turned over the organ, protects well. A triangular diaper is applied, which tends to hold the penis well up on the abdomen and keeps the suture line inverted and clean.

By this method the constricting band is removed, and also the redundancy and the secreting surface. Adhesions are eliminated, free drainage is allowed, and recurrent irritation is prevented. The corona is not necessarily exposed, and there is tissue to protect this sensitive portion. The meatus is exposed and free. This I believe is the proper technic for circumcision.

FOREIGN BODY IN A BRONCHUS. DR. R. H. SOMERS, Seattle.

A 2 year old boy was seen on the tenth day of what appeared to be a respiratory infection. The illness started with a cough, which was followed in a few days by moderate fever. Physical examination at that time revealed no pathologic condition. My first examination showed a prostrated child, with a temperature of 103 F.; the lower part of the left side of the chest was dull, with diminished sounds and no râles; the respiratory rate was 35. Twenty-four hours later the child was admitted to the hospital, where he remained for two and one-half months.

Roentgen examination indicated that fluid was probably present. Aspiration with a large needle was performed, with no success. This was repeated a few days later, still with no success, although several sites were used each time. The third attempt, with the needle inserted in the axillary line, yielded a few cubic centimeters of exceedingly thick, foul-smelling pus. The laboratory reported that the pus contained streptococci and spirilla resembling those seen in Vincent's angina. As this finding is uncommon in empyema, it suggested an infection perforating through from a bronchus, which brought into consideration the possibility of a foreign body. The most careful interrogation, however, by me and by a bronchoscopist failed to verify this surmise. The child's condition at that time and throughout the whole illness was so critical that it seemed from day to day that he could not survive; and as there was no history of a foreign body bronchoscopy was postponed until near the end. Three rib resections were done, as well as two transfusions, one intercostal drainage and probably twenty or more exploratory aspirations, in an attempt to locate some hidden pocket of pus. Sulpharsphenamine was given on the ground that it was helpful in infections with spirilla.

As drainage through the rib resections was intermittent, irrigation was resorted to, which promptly caused rupture into a bronchus, nearly proving fatal. From that time on pus literally poured from the child's mouth. In desperation, with the patient moribund, bronchoscopy was done. The main left bronchus was practically

occluded by granulation tissue, behind which there seemed to be a foreign body. It was planned to repeat the procedure in a few days, and if possible remove any foreign body. However, the child died three days later. At autopsy, the left lung was found to be a mass of small abscesses, and the pleural cavity was divided into several pockets. The original empyema had resulted from a perforation of the pulmonary infection into the pleural cavity. Lodged in the main left bronchus was a fragment of chicken bone about 0.5 cm. in diameter.

There are several points that are worth noting: 1. Empyema most frequently follows pneumonia, and in this case the history did not bring out such a factor. 2. Spirilla in the pus should make one look for an uncommon etiologic basis. 3. When one is in doubt, bronchoscopy should be done. Even in this extremely sick child no ill effects were noted. 4. It is interesting that in this case a stomach tube was used throughout the whole period, being retained through the nostril for thirty-six hours at a time and removed for twelve hours. The esophageal membrane showed no damage.

DISCUSSION

DR. A. H. SPOHN, Vancouver, B. C.: Chicken bones are dangerous to animals as well as to man, and dogs frequently die following the ingestion of chicken bones, through intestinal rather than pulmonary complications.

DR. M. D. SKINNER, Seattle: I observed the case of a child who was struck on the chest while eating peanuts. The temperature rose to 103 F., and stridor was noted. Roentgen examination revealed clouding, and because of the history bronchoscopy was done. A whole nut was removed.

DR. W. B. SEELYE, Seattle: A boy who had been given peanuts had a coughing spell. A nut which had entered a bronchus was removed successfully before any pathologic condition developed.

DR. E. J. BARNETT, Spokane, Wash.: In a child with a severe cough, roentgen examination demonstrated the diaphragm high on the left side and immobile. A foreign body was removed.

POSTURE STUDIES: A STANDARD FOR ANTERIOR POSTURE. DR. C. U. MOORE, Portland, Ore.

This paper will be published in full in a latter issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

Book Reviews

The Clinical Aspect of Chronic Poisoning by Aluminum and Its Alloys. By Leo Spira, M.D. Price, 2 shillings, 6 pence. Pp. 28. London: John Bale, Sons & Danielsson, Ltd., 1933.

The author found in the last ten years a greater number of people in England than on the continent suffering from a peculiar symptom complex embracing three main groups of symptoms: gastro-intestinal, cutaneous and general. He found a number of people with constipation, dryness in the mouth and throat, impaired appetite, nausea and, later, vomiting of every kind of food soon after it was taken. Roentgen examination revealed only colonic stasis. Certain conditions of the skin also appear with greater frequency; acute and chronic urticaria, infantile eczema, herpes and persistent furunculosis. The finger-nails become soft and brittle, lose their luster and appear opaque and thickened. The third group of symptom complexes is evidenced by frequent attacks of neuralgia and twitching of the legs, pain in the fingers and toes, arthralgia of a severe type, giddiness, excessive perspiration and anemia. Nervous symptoms comprise depression and even melancholia, loss of energy and general lassitude. One group of patients will exhibit mainly gastro-intestinal symptoms, another group cutaneous symptoms and still a third group general symptoms. The former two groups occurred or were met with so often that Spira endeavored to find an etiologic factor. In persons with previous good health who came to London, cutaneous symptoms accompanied by symptoms of the other groups developed within a few weeks or months. By a process of elimination, Spira found that food cooked in aluminum dishes was responsible for the chain of symptoms. When all aluminum pans and cooking utensils were set aside and the food was prepared in other cooking utensils, the symptoms disappeared. The best results were obtained when water free from alumina was used. The absorption and elimination of the poison accumulated in the body required large doses of high grade charcoal and an aperient. The patients remained well as long as food or drink was not contaminated with alumina.

The symptom complex described is caused by one or several irritants contained in aluminum utensils and in chlorinated or aluminized tap water.

"As the skin manifestations disappear under the described treatment, without any local applications, it seems likely that the prevailing theory that they are caused by a fungus is not tenable." The author gives illustrations showing how infantile eczema, urticaria and furunculosis were cured by merely eliminating the presence of foods cooked in aluminum dishes or the use of chlorinated tap water. The author describes the materials used in the manufacture of aluminum cooking utensils and gives the opinion of other authors regarding the toxic action of aluminum. There are three pages of bibliography.

Streptococci in Health and Disease. By Anna W. Williams and William H. Park, M.D. Price, $5. Pp. 247, with 7 plates. Baltimore: Williams & Wilkins Company, 1932.

Unlike the bibliographical compilations on streptococci written by the Thomson brothers, this book represents an interpretative summary of present knowledge of the subject. For this reason, it is valuable to the clinician as it gives him in a compact volume an understanding of the present status of streptococci as the etiologic factors in various clinical conditions, such as scarlet fever and erysipelas. The authors have been especially well fitted to write this book, since they and their associates have worked for a number of years on many of the fundamental phases of the subject about which they write. The style is simple; the analytic expositions are clear and lucid; the facts are presented in an orderly manner,

and the conclusions in the book are easily grasped. All of the authors' remarks might not be agreed with, but mooted points are so discussed and diverse and opposing opinions so justly dealt with that fault cannot be found with the fairness of their judgment. This book is one that not only should be read and laid aside, but should be referred to again and again.

Lehrbuch der Kinderheilkunde. By R. Degkwitz, A. Eckstein, E. Freudenberg with H. Brühl, F. Goebel, P. György and E. Rominger. Price, 16 marks. Pp. 611. Berlin: Julius Springer, 1933.

This German textbook on diseases of children is written by some of the outstanding men of present-day Germany whose names are familiar to practically all pediatricians the world over. The book is a compact volume without illustrations and is complete for its size. It contains little in the way of reference to articles as it is purely a textbook. The various body systems are discussed, and there is an introductory chapter on physiology, examination of the child and hygiene. The last chapter, on general therapy, terminates with a table of the most important drugs to be used in pediatrics. On the whole, the book should be useful for practitioners.

Estudios clinicos de pediatria. By Eugenio Cienfuegos. Volume 1. Pp. 261. Santiago, Chile: Imprenta "El Esfuerzo" Eyzaguirre, 1933.

This volume in Spanish deals with the nutritional disturbances of infancy, acidosis, scurvy, tuberculosis, hypothyroidism and convulsions. These subjects are given in lecture form, with several cases in each instance which illustrate the points in treatment or diagnosis that the author wishes to make. This form makes it interesting reading. It is a handy little volume for any one who desires to know the South American point of view on these conditions.

La gymnastique des tout petits. By Doris Reichmann. Price, 20 francs. Pp. 57, with 71 illustrations. Paris: Gauthier-Villars & Cie, 1933.

This booklet sets forth a rational system of active exercises for the normal infant, having as its goal not only improvement of general health, but also prevention of poor posture and deformities. It is edited for the mother, with detailed instructions, illustrations and precautions for each exercise. An outline is provided for the gradual institution of exercise.

Directory of Pediatric Societies

INTERNATIONAL

International Association of Preventive Pediatrics

President: Professor Taillens, Lausanne, Switzerland.
Secretary: Dr. P. Oltramare, rue Decandolle, Geneva, Switzerland.

International Pediatric Congress

President: Dr. George Frederic Still, 28 Queen Anne St., London, W. 1.
Secretary: Dr. Leonard K. Findlay, 61 Harley St., London, W. 1.

FOREIGN

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. Leonard G. Parsons, 58, Calthorpe Road, Birmingham, England.
Secretary: Dr. W. G. Wyllie, 33, Wimpole St., W. 1, London.

NATIONAL

American Medical Association, Scientific Assembly, Section on Diseases of Children

Chairman Dr. Alfred A. Walker, Highland Plaza Apartments, Birmingham, Ala.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Place: Cleveland. Time: June 11-15, 1934.

American Academy of Pediatrics

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.

American Child Health Association

President: Dr. Samuel McC. Hamill, 1822 Spruce St., Philadelphia.
Secretary: Dr. Philip Van Ingen, 125 E. 71st. St., New York.

American Hospital Association, Section on Children's Hospitals

President: Dr. H. C. Schumm, 425 E. Wisconsin Ave., Milwaukee.
Secretary: Miss Sophie Yoerg, 721 N. 17th St., Milwaukee.

American Pediatric Society

President: Dr. Charles A. Fife, 2104 Spruce St., Philadelphia.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid, St. Louis.
Place: Asheville, N. C. Time: May, 1934.

Canadian Society for the Study of Diseases of Children

President: Dr. Frederick F. Tisdall, 170 St. George St., Toronto, Ontario.
Secretary-Treasurer: Dr. T. G. H. Drake, 67 College St., Toronto, Ontario.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Society of Pediatric Research

President: Dr. Rustin McIntosh, College of Physicians and Surgeons, Columbia University, New York.
Secretary-Treasurer: Dr. Charles F. McKhann, Harvard Medical School, Boston.
Place: Atlantic City, N. J. Time: May, 1934.

SECTIONAL

Central States Pediatric Society

President: Dr. Julius H. Hess, 104 S. Michigan Ave., Chicago.
Secretary: Dr. A. H. Parmelee, 715 Lake St., Oak Park, Ill.
Place: Chicago. Time: Sept. 22-23, 1933.

North Pacific Pediatric Society

President: Dr. Herbert E. Coe, 509 Olive St., Seattle.
Secretary: Dr. Raymond H. Somers, Cobb Bldg., Seattle.

Southern Medical Association, Section on Pediatrics

Chairman: Dr. Hugh L. Dwyer, 406, W. 34th St., Kansas City, Mo.
Secretary: Dr. Luther W. Holloway, 117 W. Duval St., Jacksonville, Fla.
Place: Richmond, Va. Time: Nov. 14-17, 1933.

STATE

Alabama Pediatric Society

President: Dr. C. E. R. Parker, 401 S. Court St., Montgomery.
Secretary-Treasurer: Dr. John W. Simpson, 1117 S. 22d St., Birmingham.

Georgia Pediatric Society

President: Dr. Joseph Yampolsky, 311 Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Place: Atlanta. Time: October, 1933. Augusta. Time: May, 1934.

Louisiana State Pediatric Society

President: Dr. Cecil O. Lorio, 245, 3d St., Baton Rouge.
Secretary-Treasurer: Dr. Maud Loeber, Tulane University, New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Adolph G. De Sanctis, 12 E. 11th St., New York.
Secretary: Dr. George M. Retan, 459 James St., Syracuse.

Nebraska Pediatric Society

President: Dr. W. O. Colburn, 724 Sharp Bldg., Lincoln.
Secretary-Treasurer: Dr. C. G. Weigand, 1614 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Second Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. J. Buren Sidbury, 15 N. 5th St., Wilmington.
Secretary: Dr. E. K. McLean, 121 W. 7th St., Charlotte.
Place: Various children's hospitals. Time: Twice a year.

Oklahoma State Pediatric Society

President: Dr. Clark H. Hall, 117 N. Broadway, Oklahoma City.
Secretary: Dr. M. J. Searle, 108 W. 16th St., Tulsa.

South Carolina Pediatric Society

President: Dr. J. I. Waring, 77 Rutledge Ave., Charleston.
Secretary-Treasurer: Dr. Julian P. Price, Medical Bldg., Florence.

Tennessee State Pediatric Society

President: Dr. Owen H. Wilson, 706 Church St., Nashville.
Secretary: Dr. Joe T. Smith, 511 W. Church Ave., Knoxville.

Texas Pediatric Society

President: Dr. Sidney R. Kaliski, Moore Bldg., San Antonio.
Secretary-Treasurer: Dr. Frank M. Martin, 321 Medical Arts Bldg., San Antonio.
Place: San Antonio. Time: Oct. 28, 1933.

Virginia Pediatric Society

President: Dr. J. B. Stone, 2042 Park Ave., Richmond.
Secretary-Treasurer: Dr. Thomas D. Jones, Medical Arts Bldg., Second and Franklin Streets, Richmond.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. R. C. Hood, 428 W. Pike St., Clarksburg.
Secretary: Dr. Russell C. Bond, 1325 Chapline St., Wheeling.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. C. W. Burhans, 14805 Detroit Ave., Lakewood, Ohio.
Secretary: Dr. J. A. Garvin, 2009 Adelbert Road, Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Secretary: Dr. Lawrence Murray, 1870 Bloor St., W., Toronto.

Bronx Pediatric Society

President: Dr. Edward L. Benjamin, 2021 Grand Concourse, New York.
Secretary: Dr. Harry M. Schapiro, 1882 Grand Concourse.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Every Second Wednesday of each month, except June, July, August and September.

Brooklyn Pediatric Society

President Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn.
Secretary: Dr. Lewis A. Koch, 62 Pierrepont St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

Central New York Pediatric Club

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

Chicago Pediatric Society

President: Dr. Charles Schott, 48 W. Division St., Chicago.
Secretary: Dr. Bert I. Beverly, 8 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

Dallas County Pediatric Society

President: Dr. P. E. Luecke, 4105 Live Oak St., Dallas, Texas.
Secretary: Dr. R. S. Usry, 1835 Garrett Ave., Dallas, Texas.
Place: Bradford Memorial Hospital. Time: 1 p. m., first and third Saturdays of each month.

Detroit Pediatric Society

President: Dr. Bernard Bernbaum, 5057 Woodward Ave., Detroit.
Secretary: Dr. Sarah S. Schooten, 5057 Woodward Ave., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. Roger W. Dickson, 33 Ponce de Leon Ave., N. E., Atlanta.
Secretary: Dr. T. I. Willingham, 478 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Intermountain Pediatric Society

President: Dr. Helmina Jeidell, 11 Exchange Pl., Salt Lake City, Utah.
Secretary-Treasurer: Dr. Edwin R. Murphy, 9 Exchange Pl., Salt Lake City, Utah.
Place: Salt Lake City, General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. Hugh L. Dwyer, 406 W. 34th St., Kansas City.
Secretary: Dr. John Aull, 906 Grand Ave., Kansas City.

Memphis Pediatric Society

President: Dr. R. B. McCormick, 1074 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. W. D. Mims, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

Milwaukee Pediatric Society

President: Dr. Karl E. Kassowitz, 709 N. 11th St., Milwaukee.
Secretary: Dr. John H. Reynolds, 747 N. 27th St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Thomas A. Foster, 131 State St., Portland, Maine.
Secretary: Dr. Gerald Hoeffel, 319 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Martha Wollstein, Babies' Hospital of City of New York, New York.
Secretary: Dr. Harry Bakwin, 132 E. 71st St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Roland P. Seitz, 490 Post St., San Francisco.

Northwestern Pediatric Society

President: Dr. Alexander Stewart, 459 Lowry Medical Arts Bldg., St. Paul.
Secretary: Dr. E. F. Robb, 1801 Lyndale Ave., S., Minneapolis.

Philadelphia Pediatric Society

President: Dr. Joseph Stokes, 159 W. Coulter St., Philadelphia.
Secretary: Dr. James E. Bowman, 4091 Comly St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

Pittsburgh Pediatric Society

President: Dr. Henry C. Flood, 119 S. Highland Ave., Pittsburgh.
Secretary: Dr. E. R. McCluskey, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to April, inclusive.

Richmond Pediatric Society

President: Dr. F. Waring Lewis, Professional Bldg., Richmond, Va.
Secretary-Treasurer: Dr. A. S. Hurt, Jr., 2618 Grove Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. H. F. Rowley, 176 S. Goodman St., Rochester, N. Y.
Secretary: Dr. J. M. Parker, 26 S. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month from October to May.

Rocky Mountain Pediatric Society

President: Dr. J. A. Schoonover, Republic Bldg., Denver.
Secretary: Dr. Arthur L. Esserman, Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7 p. m.

St. Louis Pediatric Society

President: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Katherine Bain, Beaumont Bldg., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Albert S. McCown, 509 Olive St., Seattle.
Secretary: Dr. Frank H. Douglass, Medical-Dental Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, 7 p. m.

Southwestern Pediatric Society

President: Dr. James E. Harvey, 60 S. Lake Ave., Pasadena, Calif.
Secretary: Dr. E. Earl Moody, 3780 Wilshire Blvd., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Gustave F. Weinfeld, Moraine Hotel, Highland Park, Ill.
Secretary: Dr. John P. Parsons, 320 S. Division St., Ann Arbor, Mich.
Place: Ann Arbor Mich. Time: November, 1933.